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Prevalence of multimorbidity with frailty and associations with socioeconomic position in an adult population: findings from the cross-sectional HUNT Study in Norway.

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Multimorbidity. Frailty. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: To explore prevalences and occupational class inequalities of two measures of multimorbidity with frailty.

Design: Cross-sectional study.

Setting: The Nord-Trøndelag Health Study (HUNT), Norway, a total county population health survey, 2006-2008.

Participants: Participants older than 25 years, with complete questionnaires, measurements and occupation data, were included.

Outcomes: ≥2 of 51 multimorbid conditions with ≥1 of 4 frailty measures (poor health, mental illness, physical impairment or social impairment) and ≥3 of 51 multimorbid conditions with ≥2 of 4 frailty measures.

Analysis: Logistic regression models with age and occupational class, were specified for each sex separately.

Results: Of 41193 adults, 38027 (55% women; 25-100 years old) were included. 39% had ≥2 multimorbid conditions with ≥1 frailty measure, and 17% had ≥3 multimorbid conditions with ≥2 frailty measures. Prevalence differences in percentage points of those in high vs low occupational class with ≥2 multimorbid conditions and ≥1 frailty measure, were 17 (95% CI,14 to 20) in women and 5 (1 to 9) in men at 30 years; 15 (13 to 17) in both sexes at 55 years; and 3 (-3 to 9) in women and 14 (9 to 18) in men at 80 years. In those with ≥3 multimorbid conditions and ≥2 frailty measures, prevalence differences were 8 (6 to 10) in women and 2 (0 to 4) in men at 30 years; 10 (8 to 11) in women and 9 (8 to 11) in men at 55 years, and 4 (-1 to 10) in women and 6 (1 to 10) in men at 80 years.

Conclusion: Multimorbidity with frailty is common and social inequalities persist until age 80 years in women and throughout the lifespan in men. To manage complex multimorbidity, strategies for proportionate universalism in medical education, health care, public health prevention and promotion seem necessary.

ARTICLE SUMMARY

Strengths and limitations of this study

1. The HUNT Study is a large total county population general health survey with a multitude of variables, suitable to estimate prevalences of multimorbidity and frailty by self-reports and clinical measurements.
2. Occupation is used as a marker for socioeconomic position, enabling international comparison.
3. Sex-specific occupational class differences in multimorbidity with frailty are reported with both absolute and relative measures of inequality
4. As a secondary analysis, the measures in this study need to be adjusted to fit previously collected data.
5. In particular, the original data lacked information of chronicity of conditions, which may lead to overestimation of multimorbidity.

INTRODUCTION

Multimorbidity, the co-occurrence of multiple, chronic conditions, where none is more central,[1] is increasingly prevalent and becoming the norm.[2-4] Multimorbidity is associated with high health care utilization[5] and challenges clinicians in a fragmented health care system, aided by single disease guidelines.[6] The treatment burden to patients is often substantial including lowered ability to self-care.[6] Ways to harmonize guidelines to fit multimorbidity[7 8] and manage patients with multimorbidity in clinical practice[6] have been explored, and specific multimorbidity care guidelines are emerging.[9 10]

Multimorbidity alone may not imply a need for complex, multidisciplinary care.[11] Sociodemographic characteristics, individual health and social experiences, and mental and somatic health characteristics[12], increase patient complexity. The British National Institute for Health and Care Excellence (NICE) guideline[10] recommends a multimorbid approach to care in various contexts, including mixed mental and somatic multimorbidity and multimorbidity with frailty. Multimorbidity is defined as two or more long-term, single-count health conditions.[10]

Frailty is considered a dynamic state, involving loss of function in spheres such as physical, psychological, and social domains,[13] resulting in lower reserve capacity[14] and increased vulnerability for adverse outcomes.[13] The NICE guideline proposes identification of frailty through observation of a low gait speed or poor self-rated health or by scoring a frailty scale combining demographic characteristics and multidimensional impairments.[10]

Social differences in health are established; low socioeconomic position is associated with poorer health outcomes in Nordic countries[15] and globally.[16] Multimorbidity and frailty are no exception. Common determinants are female sex, socioeconomic deprivation and higher age.[4 17 18] However, most patients with multimorbidity are younger than 65 years,[19] and frailty is associated with multimorbidity and mortality from middle age onward.[18] The NICE guideline emphasizes assessment of multimorbid approach to care for adults of all ages but does not take into account social position.

There are numerous operational definitions of multimorbidity and frailty. The literature suggests that multimorbidity, defined as three or more single health conditions, increases specificity especially in older age groups.[20 21] Most frailty scales require multidimensional loss of function to identify frail individuals.[22]

The overall purpose of this study is to identify how many in a general adult population is likely to need complex, multidisciplinary care as given by one of the contexts suggested by the NICE guideline; multimorbidity with frailty. Two measures will be assessed, one in line with the guideline (two conditions of multimorbidity plus one dimension of frailty) and the other with expected increased specificity (three conditions of multimorbidity plus two dimensions of frailty). The second aim is to examine associations of these measures according to age, sex, and socioeconomic position.

MATERIALS AND METHODS

Reporting statement

The STROBE cross sectional reporting guidelines[23] were used for reporting of this observational study.

Study design and population

This cross-sectional study use data from the third wave in the Norwegian HUNT Study (the HUNT3 Survey, 2006-2008). Details on data collection and the cohort profile of this total county population health survey was published previously.[24] In brief, 93860 residents older than 20 years were invited to participate.

Figure 1 presents the sample selection for this analysis. Eligible participants completed all major parts of the HUNT3 Survey; the main, age- and sex-specific questionnaires; interviews; and measurements. 52663 individuals were excluded due to no or incomplete participation. Four missed information on participation. 1569

respondents were younger than 25 years and were excluded on the assumption that the highest level of occupational class may not yet be obtained by those in this age group. One missed information on age. 1571 individuals missed information on occupation, while 25 people had “unspecified occupation” and was excluded. 38027 participants were included in the final sample.

Demographic and Sociodemographic Characteristics

Sex and age at participation in the HUNT3 Survey was constructed by the HUNT Databank. Occupational class was used as indicator of socioeconomic position.[25] In the HUNT3 Survey interview, all participants were asked, “What is/was the title of your main occupation?” Free-text answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,[26] which is based on the International Standard Classification of Occupations-88.[27] Occupational socioeconomic position was operationalized using occupation only, corresponding to a simplified version of the European Socio-economic Classification scheme.[28] Collapsed to a 3-class version, the high level represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and supervisory occupations. The middle class consist of small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The low level contains lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. Details are provided in appendix A.

Outcomes

Multimorbidity

The construction of 51 single, chronic conditions from the HUNT3 Survey data, is described in appendix B. In this study, a simple, non-weighted summary score was generated and two multimorbidity variables created, with cutoff values of at least 2 of 51 and 3 of 51 conditions.

Frailty

Four dimensions of frailty were operationalized from six original variables:

1. General health status, defined as those reporting the answers “poor” or “not so good” (vs “good” and “very good”) to the single question “How is your health at the moment?”
2. Mental health status, included those reporting symptoms of anxiety and/or depression, on the Hospital Anxiety and Depression Scale. The HUNT Databank calculated a total score for subscales of anxiety and depression, if all items for anxiety and depression, respectively, were answered. In this study, cutoff was set at 8/21 points for both conditions[29] and a combined variable was created.
3. Physical impairment was identified by combining those reporting “yes” (vs “no”) in response to the question, “Do you suffer from any long-term (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” and reporting either motor ability, vision, or hearing impairment to a moderate or severe degree.
4. Social impairment was derived from answers to the single question, “To what extent has your physical health or emotional problems limited you in your usual socializing with family or friends during the last 4 weeks?” Included were those reporting “much” and “not able to socialize” (vs “not at all,” “very little,” or “somewhat”).

A summary score was generated and two frailty variables created, with cutoff values of at least 1 of 4 and 2 of 4 frailty measures with impairment.

Multimorbidity with frailty

The two final outcome variables, were created by combining self-reported multimorbidity and frailty as at least 2 of 51 chronic health conditions plus impairment in 1 of 4 dimensions of frailty and 3 of 51 chronic health conditions plus impairments in 2 of 4 dimensions of frailty.

Statistical analysis

We used cross-tables to identify sociodemographic characteristics by occupational class (table 1) and by multimorbidity with frailty, stratified by sex (table 2).

Associations between occupational class and the two measures of multimorbidity with frailty were analyzed using logistic regression, adjusted for age and sex. All models were stratified by sex and included occupational class, continuous age, age squared, and an interaction term between occupational class and age. Likelihood ratio tests were used to compare models.

Given the high prevalence of multimorbidity with frailty and the knowledge that odds ratios will deviate from relative risks,[30] we used postestimation commands to obtain prevalence differences and prevalence ratios[31] between the occupational classes with high occupational class as the reference category. The prevalence difference is the difference in mean predicted probability, and prevalence ratio is the ratio between the mean predicted probabilities while holding other covariates constant.[31] Prevalence difference and prevalence ratio between occupational groups were calculated at age 25 to 100 years in 5-year intervals (appendix C). Table 3 presents calculations at ages 30, 55 and 80 years, reported with 95% confidence intervals. We performed complete case analysis and used Stata version 15.1 (StataCorp. College Station, TX, USA) to analyze the data.

Patient and public involvement

This study is a secondary analysis of a cohort study run in 2006-2008. Multimorbidity is a universal topic, not represented by any particular patient group, thus no patient or public representative were involved in designing the study.

RESULTS

38027 individuals, older than 25 years, who had completed all major parts of the HUNT3 Survey and had data on occupation, comprised the final sample for this study (fig. 1). Further sociodemographic characteristics, is presented in table 1.

Table 1. Sex and age distribution by occupational class.

	Occupational class							
	High		Middle		Low		Total	
	Freq.	(%)	Freq.	(%)	Freq.	(%)	Freq.	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Female	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
Male	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, yr.								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

Abbreviations: freq., frequency, yr., years; SD, standard deviation

The low occupational class is the largest overall, with 49% (n=18814 of 38027) of the sample. Furthermore, the low occupational class is the largest in absolute numbers in all age groups. There are more women (n=10922 of 18814 [58%]) than men (n=7892 of 18814 [42%]) in the low occupational class and in total with 20813 women (of 38027 [55%]) and 17214 men (of 38027 [45%]). The group aged 45 to 64 years constitutes the largest age group in all occupational classes and overall (n=18206 of 38027 [48%]).

Table 2. Frequency distribution of two definitions of multimorbidity with frailty across occupational classes and age groups, stratified by sex.

	Women						Men					
	Two conditions of multimorbidity and one dimension of frailty*						**Two conditions of multimorbidity and one dimension of frailty***					
	No, freq.	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**	**No, freq.**	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**
Total	12 304	(59)	8 482	(41)	20 813	(100)	10 826	(63)	6 378	(37)	17 214	(100)
Occupational class												
High	3 222	(72)	1 282	(28)	4 505	(100)	3 220	(72)	1 242	(28)	4 465	(100)
Middle	3 370	(63)	2 009	(37)	5 386	(100)	2 995	(62)	1 860	(38)	4 857	(100)
Low	5 712	(52)	5 191	(48)	10 922	(100)	4 611	(58)	3 276	(42)	7 892	(100)
Age, years												
25-44	4 298	(72)	1 680	(28)	5 981	(100)	3 075	(78)	867	(22)	3 943	(100)
45-64	5 712	(58)	4 122	(42)	9 840	(100)	5 398	(65)	2 967	(35)	8 366	(100)
65-74	1 615	(51)	1 548	(49)	3 168	(100)	1 681	(54)	1 409	(46)	3 093	(100)
75-100	679	(37)	1 132	(62)	1 824	(100)	672	(37)	1 135	(63)	1 812	(100)
Mean (SD)	52	(14)	58	(14)	54	(14)	54	(14)	61	(14)	56	(14)
	Three conditions of multimorbidity and two dimensions of frailty*						**Three conditions of multimorbidity and two dimensions of frailty***					
	No, freq.	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**	**No, freq.**	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**
Total	16 983	(82)	3 803	(18)	20 813	(100)	14 367	(83)	2 837	(16)	17 214	(100)
Occupational class												
High	4 029	(89)	475	(11)	4 505	(100)	3 977	(89)	485	(11)	4 465	(100)
Middle	4 491	(83)	888	(16)	5 386	(100)	3 995	(82)	860	(18)	4 857	(100)
Low	8 463	(77)	2 440	(22)	10 922	(100)	6 395	(81)	1 492	(19)	7 892	(100)
Age, years												
25-44	5 378	(90)	600	(10)	5 981	(100)	3 651	(93)	291	(7)	3 943	(100)
45-64	7 920	(80)	1 914	(19)	9 840	(100)	7 024	(84)	1 341	(16)	8 366	(100)
65-74	2 449	(77)	714	(23)	3 168	(100)	2 472	(80)	618	(20)	3 093	(100)
75-100	1 236	(68)	575	(32)	1 824	(100)	1 220	(67)	587	(32)	1 812	(100)
Mean (SD)	53	(14)	60	(14)	54	(14)	55	(14)	63	(13)	56	(14)

Abbreviations: freq., frequency; yr., years; SD, standard deviation

*In total, 27 women and 10 men miss data on both measures of multimorbidity with frailty.

Overall, 39% met the criteria of having at least two conditions of multimorbidity with one dimension of frailty (41% of women, 37% of men) and 17% met the criteria of three-condition multimorbidity with two dimensions of frailty (18% of women and 16% of men) (Table 2).

Proportions of multimorbidity with frailty increased with lower occupational rank, for both definitions and in both sexes. The increase from high to low occupational class, for two-condition multimorbidity with one dimension of frailty, was 28% to 48% in women and 28% to 42% in men. Corresponding numbers for three-condition multimorbidity with two dimensions of frailty, were 11% to 22% in women and 11% to 19% in men. The absolute numbers with any definition of multimorbidity with frailty, were greater in the low occupational class, than any age group.

Proportions of joint multimorbidity with frailty increased with age in both sexes, regardless of definition. Two-condition multimorbidity with one dimension of frailty was reported by 28% of women and 22% of men 25- to 44-year-old, increasing to 62% of women and 63% of men 75- to 100-year-old. Equivalent numbers for three-condition multimorbidity with two dimensions of frailty were 10% of women and 7% of men, increasing to 32% in both sexes. In absolute numbers, most individuals with co-present multimorbidity and frailty were 45- to 64-year-old.

Table 3. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) between occupational class and multimorbidity with frailty, stratified by sex.

		Women				Men			
Age, years	**Occupational class**	**Two conditions of multimorbidity and one dimension of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00		0.00		1.00		0.00	
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
55	High	1.00		0.00		1.00		0.00	
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
80	High	1.00		0.00		1.00		0.00	
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.17)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
Age, years	**Occupational class**	**Three conditions of multimorbidity and two dimensions of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00		0.00		1.00		0.00	
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
55	High	1.00		0.00		1.00		0.00	
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.07)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
80	High	1.00		0.00		1.00		0.00	
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)

Table 3 shows prevalence differences and prevalence ratios for each definition of multimorbidity with frailty between occupational groups for women and men at the ages 30, 55, and 80 years.

Prevalence differences in percentage points (pp) for two-condition multimorbidity with one dimension of frailty between high and low occupational classes were; at 30 years, 17 (14 to 20) pp in women and 5 (1 to 9) pp in men; at 55 years, 15 (13 to 17) pp in both sexes, and at 80 years, 3 (-3 to 9) pp in women and 14 (9 to 18) pp in men. Compared with the high occupational group, the prevalence ratio for the low occupational class for two-condition multimorbidity with one dimension of frailty, was; at 30 years, 2.09 (1.76 to 2.47) for women and 1.32 (1.04 to 1.67) for men; at 55 years, 1.48 (1.38 to 1.58) for women and 1.60 (1.48 to 1.72) for men, and at 80 years 1.05 (0.95 to 1.16) for women and 1.27 (1.15 to 1.39) for men.

Correspondingly, prevalence differences in percentage points between high and low occupational groups for three-condition multimorbidity with two dimensions of frailty, were; at 30 years, 8 (CI: 6 to 10) pp in women and 2 (CI: 0 to 4) pp in men; at 55 years, 10 (CI: 8 to 11) pp in women and 9 (CI: 8 to 11) pp in men, and at 80 years, 4 (CI: -1 to 10) pp in women and 6 (CI: 1 to 10) pp in men. Prevalence ratio, comparing the low occupational class with the highest occupational class for three-conditions multimorbidity with two conditions of frailty, was; at 30 years, 3.59 (1.43 to 5.08) for women and 1.60 (1.02 to 2.51) for men; at 55 years 1.78 (1.59 to 2.00) for women and 2.05 (1.80 to 2.33) for men, and finally at 80 years, 1.16 (0.94 to 1.42) for women and 1.22 (1.04 to 1.44) for men.

DISCUSSION

Main results

In this adult population health study, multimorbidity with frailty was common as 39% met the criteria of two-condition multimorbidity plus one dimension of frailty and 17% met the criteria of three-condition multimorbidity plus two dimensions of frailty. Proportions increased with lower occupational class, higher age and female sex from 25 to 74 years, but was common across age groups in both sexes. Occupational inequalities were consistent in both sexes until 80 years of age.

Comparison with existing literature

Investigating two measures of multimorbidity with frailty in one sample offers a unique direct comparison of occurrences and socioeconomic gradients. Lower overall prevalence for the stricter measure three-condition multimorbidity with two dimensions of frailty, is expected. Defining multimorbidity by three or more conditions differentiates into older age[20 21]. The joint measure multimorbidity and frailty, show the same tendency, as 62% of 75- to 100-year-olds met the criteria of at least two-condition multimorbidity with one dimension of frailty, while 32% reported three-condition multimorbidity with two dimensions of frailty. In line with individual studies on multimorbidity[19] and frailty[18], most individuals with co-present multimorbidity and frailty are younger than 64 years. A recent commentary[11] emphasized exploring multimorbidity guidelines and frailty as part of multimorbidity's complexity. Overlap of multimorbidity and frailty has been studied extensively,[32] but was beyond the scope of this study. Other researchers have focused on separating the concepts.[33] We have identified one study that evaluated the NICE guideline's polypharmacy approach to define multimorbidity on several outcomes,[34] however, none that have studied prevalence and social determinants of multimorbidity with frailty. Low social position, older age, and female sex are known common determinants of multimorbidity[4 17] and frailty.[18] We therefore argue that the direction of the sociodemographic determinants in this study are as expected. The sizes of the gradients, however, have not been comparable with other studies.

Mechanisms to explain findings

The aggregation of ill health, multimorbidity and frailty included, in lower socioeconomic classes is explained by numerous theories. Unequal distribution of power, income and resources, result in fundamental different conditions of daily life and health-threating exposures yielding inequalities in health.[16] Persisting health inequalities in assumed egalitarian Nordic countries, is partly understood as mortality selection, where given the well-developed health care and welfare systems, frail individuals survive, but likely end up in a low social position.[15] Further, the risk factor smoking, overall morbidity and mortality decreases at a higher rate among higher than lower social classes.[15] In this study, the demographic age distribution may in part explain the high

number of 45- to 64-years old with co-present multimorbidity and frailty. Additionally, incidence of new conditions, is associated with count of conditions at baseline, as well as age,[4] thus individuals in lower occupational classes may aggregate conditions faster. The bidirectional association of health and occupation, may explain higher occupational class prevalence ratios in younger individuals.[25] Lower ratios by increasing age are expected, since multimorbidity with frailty is more common[35] with advancing age. Finally, survival bias justifies diminishing occupational differences at age 80 years.

Strengths and limitations

Materials and methods meet the standards of studies on multimorbidity, frailty, and social health inequalities, strengthening this study. In multimorbidity studies, population-based health surveys are the most frequent study design,[36] and prevalence estimates from self-reports are justified when studying large samples.[20] Deriving the condition count multimorbidity measures from a complete list of single-entity conditions, is shown to yield proper prevalence estimates.[21] A multidimensional frailty measure agrees with common frailty scales.[22] In descriptive studies, any measure of socioeconomic position will reveal health inequalities, if such exists.[25] Occupation is an established marker for socioeconomic position,[25] in which this study had individual data classified to facilitate international comparison. Finally, socioeconomic differences are explored with both absolute and relative measures[15] and presented by sex.[17]

There are always limitations in secondary analysis of data collected a priori and not for the purpose of the current study. Measures of multimorbidity and frailty are also manifold, and operationalizations were adjusted to fit the available data. This challenges the external validity and comparability between studies, however, is sought reduced through transparency of morbidities included and construction of variables. A majority of included multimorbidity conditions do not contain information regarding duration. Thus, reported prevalence of multimorbidity may be overestimated and not represent true chronicity. Frailty was measured solely as self-report, an approach that may underestimate overall prevalence[37] and overestimate proportion among women compared to men.[37] Lastly, this study had data on main occupation only, which may obscure current social context,[25] and underestimate socioeconomic inequalities. Attendance in the HUNT3 Survey varied by age, sex, and social position,[38] still, the HUNT study is considered representative for Norway as a whole.[39] Depression hindered participation,[38] which may yield underestimation of both multimorbidity and frailty. An overall bias towards healthy elders is probable, since eligibility depended on attendance at a screening station.

Implications for clinical practice and policy makers

This study aimed to quantify the total prevalence of adults who might need complex, multidisciplinary care assessed as the joint measure multimorbidity and frailty. In a clinical context, the definition of at least three-condition multimorbidity with two dimensions of frailty to detect individuals for whom to initiate a multimorbid approach to care, seems more feasible. Despite acknowledgement of the association of multimorbidity and frailty with age, sex, and socioeconomic position, guidelines and interventions have yet to take this into account in assessment and management for multimorbidity.[40] Based on literature and reproduction of social gradients in our study, we suggest that clinicians consider evaluation of multimorbidity and frailty in younger age groups with social context in mind. Further research on implementation of the multimorbid approach to care model and mortality is needed before recommending changing inclusion criteria in a guideline. Since multimorbidity is becoming the norm, the organization of health care should reform to fit person-centred, coordinated, multidisciplinary care. To prevent cases of multimorbidity and frailty and minimize social discrepancies, both universal and targeted life cycle approaches seem necessary. Frailty is independently associated with mortality, adjusted for multimorbidity,[18] and is reversible.[41] Thus detection of frailty is relevant for both public health and clinical purposes.

Future research

Some forms of biases are possible for both multimorbidity, frailty and social position, and a careful interpretation of findings is warranted. However, multimorbidity with frailty is common in this general population and with occupational inequalities throughout adulthood, even with stricter definitions. This adds knowledge to

the public health literature about the sociodemographic distribution of multimorbidity with frailty in younger age groups, as well as very old individuals. On this background, we recommend exploring the sociodemographic distribution of alternative measures on multimorbidity, aiming to detect individuals suspected in high need of complex, multidisciplinary health care. Furthermore, such measurements can be compared as prognostic factors for health care utilization and mortality.

CONCLUSION

Multimorbidity with frailty are common from young adulthood onward, with consistent socioeconomic inequalities until 80 years old. Prevention will require a proportionate universal approach on social determinants of health throughout the entire life span. The crucial need for person-centered multimorbid approach to care that acknowledges social context, demands reforms in health care organizational structure, medical education, and treatment. Further research on competing measures of high-need multimorbidity and the association of these factors with health care utilization and mortality should be explored by socioeconomic position, age and sex.

FIGURES

Fig. 1. Flowchart for sample selection: inclusion and exclusion criteria and missing data.

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COMPETING INTERESTS

None declared.

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AUTHOR CONTRIBUTIONS

KHV, ERS and KD conceptualized the study and all authors contributed to its design. KHV has analysed the data under supervision of ERS and all authors have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by ERS, KD and PB. All authors have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

LICENSE STATEMENT

PATIENT CONSENT

Participation in all parts of the HUNT3 Survey was voluntary, and written informed consent was obtained from all participants.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Operationalizing socioeconomic position.

Appendix B: Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix C: Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational class and joint multimorbidity and frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

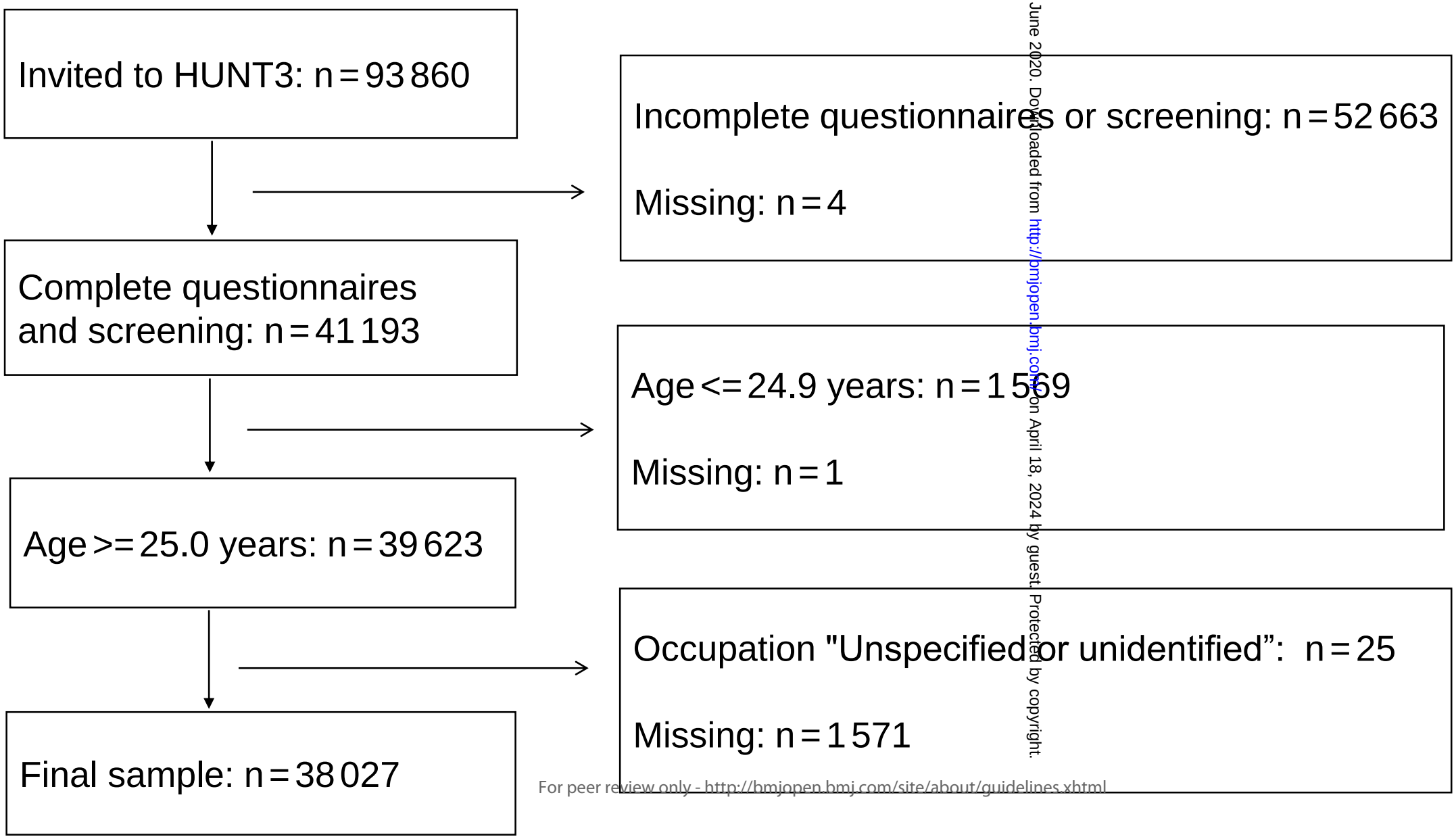
REFERENCES

1. Boyd CM, Fortin M. Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design? *Public Health Rev* 2010;32(2):451-74. doi: 10.1007/bf03391611
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time trends in prevalence of chronic diseases and multimorbidity not only due to aging: data from general practices and health surveys. *PLoS One* 2016;11(8):e0160264. doi: 10.1371/journal.pone.0160264
3. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14 Suppl 1(sup1):28-32. doi: 10.1080/13814780802436093 [published Online First: 2008/10/31]

4. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 1998;51(5):367-75. doi: 10.1016/s0895-4356(97)00306-5 [published Online First: 1998/06/10]
5. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011;28(5):516-23. doi: 10.1093/fampra/cmr013 [published Online First: 2011/03/26]
6. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. *BMJ* 2015;350:h176. doi: 10.1136/bmj.h176 [published Online First: 2015/02/04]
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. *BMJ* 2012;345:e6341. doi: 10.1136/bmj.e6341 [published Online First: 2012/10/06]
8. Muth C, Kirchner H, van den Akker M, et al. Current guidelines poorly address multimorbidity: pilot of the interaction matrix method. *J Clin Epidemiol* 2014;67(11):1242-50. doi: 10.1016/j.jclinepi.2014.07.004 [published Online First: 2014/09/14]
9. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). *Health Policy* 2018;122(1):4-11. doi: 10.1016/j.healthpol.2017.09.006 [published Online First: 2017/10/03]
10. National Institute for Health and Care Excellence. Multimorbidity: clinical assessment and management. NICE guideline [NG56]. https://www.nice.org.uk/guidance/ng56, 2016.
11. Nicholson K, Makovski TT, Griffith LE, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. *J Clin Epidemiol* 2019;105:142-46. doi: 10.1016/j.jclinepi.2018.09.008 [published Online First: 2018/09/27]
12. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *J Comorb* 2012;2:1-9. doi: 10.15256/joc.2012.2.15 [published Online First: 2012/10/10]
13. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. In search of an integral conceptual definition of frailty: opinions of experts. *J Am Med Dir Assoc* 2010;11(5):338-43. doi: 10.1016/j.jamda.2009.09.015 [published Online First: 2010/06/01]
14. Schuurmans H, Steverink N, Lindenberg S, et al. Old or frail: what tells us more? *J Gerontol A Biol Sci Med Sci* 2004;59(9):M962-5. doi: 10.1093/gerona/59.9.m962 [published Online First: 2004/10/09]
15. Huijts T, Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. *Eur J Public Health* 2009;19(5):452-3. doi: 10.1093/eurpub/ckp103 [published Online First: 2009/07/10]
16. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health. Geneva2008:9.
17. Violan C, Foguet-Boreu Q, Flores-Mateo G, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One* 2014;9(7):e102149. doi: 10.1371/journal.pone.0102149 [published Online First: 2014/07/23]
18. Hanlon P, Nicholl BI, Jani BD, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. *The Lancet Public Health* 2018;3(7):e323-e32. doi: 10.1016/s2468-2667(18)30091-4
19. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2 [published Online First: 2012/05/15]
20. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337 [published Online First: 2012/03/14]
21. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ Open* 2014;4(7):e004694. doi: 10.1136/bmjopen-2013-004694 [published Online First: 2014/07/13]
22. Theou O, Brothers TD, Mitnitski A, et al. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. *J Am Geriatr Soc* 2013;61(9):1537-51. doi: 10.1111/jgs.12420 [published Online First: 2013/09/14]

23. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014;12(12):1495-9. doi: 10.1016/j.ijsu.2014.07.013 [published Online First: 2014/07/22]
24. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. *Int J Epidemiol* 2013;42(4):968-77. doi: 10.1093/ije/dys095 [published Online First: 2012/08/11]
25. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull* 2007;81-82(1):21-37. doi: 10.1093/bmb/ldm001 [published Online First: 2007/02/08]
26. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
27. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
28. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518
29. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
30. Sedgwick P. Relative risks versus odds ratios. *Bmj-British Medical Journal* 2014;348(feb07 2):g1407-g07. doi: 10.1136/bmj.g1407
31. Norton EC, Miller MM, Kleinman LC. Computing adjusted risk ratios and risk differences in Stata. *Stata J* 2013;13(3):492-509. doi: Doi 10.1177/1536867x1301300304
32. Vetrano DL, Palmer K, Marengoni A, et al. Frailty and Multimorbidity: A Systematic Review and Meta-analysis. *J Gerontol A Biol Sci Med Sci* 2019;74(5):659-66. doi: 10.1093/gerona/gly110 [published Online First: 2018/05/05]
33. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;59(3):255-63. doi: 10.1093/gerona/59.3.m255 [published Online First: 2004/03/20]
34. Sasseville M, Smith SM, Freyne L, et al. Predicting poorer health outcomes in older community-dwelling patients with multimorbidity: prospective cohort study assessing the accuracy of different multimorbidity definitions. *BMJ Open* 2019;9(1):e023919. doi: 10.1136/bmjopen-2018-023919 [published Online First: 2019/01/07]
35. Scanlan JP. Guest Editorial. *Chance* 2013;19(2):47-51. doi: 10.1080/09332480.2006.10722787 [published Online First: 02 Aug 2013]
36. Willadsen TG, Bebe A, Koster-Rasmussen R, et al. The role of diseases, risk factors and symptoms in the definition of multimorbidity - a systematic review. *Scand J Prim Health Care* 2016;34(2):112-21. doi: 10.3109/02813432.2016.1153242 [published Online First: 2016/03/10]
37. Theou O, O'Connell MD, King-Kallimanis BL, et al. Measuring frailty using self-report and test-based health measures. *Age Ageing* 2015;44(3):471-7. doi: 10.1093/ageing/afv010 [published Online First: 2015/02/18]
38. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012;12:143. doi: 10.1186/1471-2288-12-143 [published Online First: 2012/09/18]
39. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk epidemiologi* 2003;13(1):19-32.
40. Smith SM, Soubhi H, Fortin M, et al. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *BMJ* 2012;345:e5205. doi: 10.1136/bmj.e5205 [published Online First: 2012/09/05]
41. Gill TM, Gahbauer EA, Allore HG, et al. Transitions between frailty states among community-living older persons. *Arch Intern Med* 2006;166(4):418-23. doi: 10.1001/archinte.166.4.418 [published Online First: 2006/03/01]

Fig. 1. Flowchart for sample selection: inclusion and exclusion criteria and missing data.



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Appendix A
Operationalizing socioeconomic position.

In the HUNT3 Survey interview, all participants were asked: “What is/was the title of your main occupation?” Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,(1) which is based on the European Union’s version of the *International Standard Classification of Occupations-88.*(2)

The standard categorizes occupations according to skill level and specialization, degree of independence, and manual labor but not social position.(1) Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.(3) The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only(3), as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.(3)

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string “011” changed to numeric value “11,” which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).(3)

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits). See tab 1.

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3

to 6, and “low” combining 7 to 9. (3) The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

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Table A1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		**European Socio-economic**		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

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References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway; 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm.
3. Rose D, Harrison E. The European Socio-economic Classification: A New Social Class Schema for Comparative European Research2007. 459-90 p.

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Appendix B

Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Original questionnaires, English version.

The main questionnaire (Questionnaire 1).
https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

The age- and sex-specific questionnaire (Questionnaire 2).
https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

General comments.

Chronicity.

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care). (1)

Missing.

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

1. Main questionnaire.

1.1. Hearing impairment.

Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no.
Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).
Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

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1.2. "20 Diseases": Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis.

Cluster text: "Have you had or do you have any of the following:
Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain hemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis?"
Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

2. Sex- and age-differentiated questionnaire.

2.1. Headache.

Seven questions in one block. Question 1: "Have you had headaches in the last year?" Yes/no.

2.1.1. Migraine without aura.

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:

a. "What is the average strength of your headaches?" 1=Mild, 2=Moderate, 3=Strong.
   Recoded to dichotomous variable, where 1=Moderate/Strong.
b. "How long does the headache usually last?" 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days.
   Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
c. Cluster text: "Are the headaches usually characterized or accompanied by
   - Throbbing/thumping pain?" Yes, no.
   - Pain on one side of the head?" Yes, no.
   - Worsening with physical activity?" Yes, no.
   - Nausea and/or vomiting?" Yes, no.
   - Hypersensitivity to light and/or noise?" Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise). (2)
Chronicity is assumed based on medical knowledge and clinical experience.

2.1.2. Chronic headache.

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:

a. "If yes (headache in the last year): What type of headache? Migraine, other."
   The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
b. "Average number of days a month with headaches:"
   1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days.
   Recoded to dichotomous variable, where 1= More than 14 days.

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Included as case with chronic headache were those reporting “other” type of headache and an average frequency of more than 14 days per month.
Chronicity is assumed based on medical knowledge and clinical experience.

2.2. Pain.

Index question: “In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?” Yes, no.
The follow-up question “If yes: Where have you had this pain or stiffness?” was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

2.2.1. Chronic widespread pain.

Dichotomous variables were made for each major body area: trunk (neck, upper and lower back), upper limb (shoulder, elbow, hand), and lower limb (hip, knee, foot/ancle), where for each 1=At least one painful location.
A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.(3)

2.2.2. Chronic, local pain.

Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

2.3. Thyroidal disease.

Cluster text: “Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?” Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

2.4. Irritable bowel syndrome.

Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:

a. “In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
b. “Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
c. “Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
d. “Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria. (4, 5)

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2.5. Gastro-oesophageal reflux disease.

Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much).
Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months. (6)

2.6. Anxiety.

Instrument variable: Hospital Anxiety and Depression Scale.(7) Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered.
Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety.(8-10)
Chronicity is assumed based on medical knowledge and clinical experience.

2.7. Depression.

Instrument variable: Hospital Anxiety and Depression Scale.(7) Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.
Depression was defined as HADS-D score >=8/21, indicating mild or possible depression.(8-10)
Chronicity is assumed based on medical knowledge and clinical experience.

2.8. Chronic insomnia.

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: “How often in the last 3 months have you

a. “Had difficulty falling asleep at night?” Never/seldom, sometimes, several times a week.
b. “Woken up repeatedly during the night?” Never/seldom, sometimes, several times a week.
c. “Woken too early and couldn’t get back to sleep?” Never/seldom, sometimes, several times a week.

Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.(11)

2.9. Alcohol use disorder.

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.(12) The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.(13)
Chronicity is assumed based on medical knowledge and clinical experience.

2.10. Dental health problem.

One question: “How would you say your dental health is?” Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health.
Chronicity is assumed based on medical knowledge and clinical experience.

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2.11. Menopausal hot flashes.

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
“Do you have/have you had hot flashes due to menopause?” During the day, during the night, day and night, haven’t had any.
“If you have had hot flashes, how would you describe them?” Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity.
Chronicity is assumed based on medical knowledge and clinical experience.

2.12. Nocturia.

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.
“How many times do you get up during the night to urinate?” None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.(14)
Chronicity is assumed based on medical knowledge and clinical experience.

2.13. Urine incontinence.

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.(15)
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. “If yes”:
“How often do you have involuntary loss of urine?” Less than once a month, once or more per month, once or more per week, every day and/or night
“How much urine do you leak each time?” Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.(15)
Urine incontinence were included if severe to very severe.
Chronicity is assumed based on medical knowledge and clinical experience.

2.14. Prostate symptoms.

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale (16) was slightly modified in HUNT3,(17) becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity; summary score >=8 points.(16)
Chronicity is assumed based on medical knowledge and clinical experience.

2.15. Eye diseases.

The age group 20-29 years were excluded.
Cluster text: “Do you have any of the following eye conditions?” Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.

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3. Measurements.

3.1. Obesity.

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m^2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).(18, 19)
Chronicity is assumed based on medical knowledge and clinical experience.

3.2. Hypertension.

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.
Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures.
Chronicity is assumed based on medical knowledge and clinical experience.

3.3. Hypercholesterolemia

Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.(20)
Chronicity is assumed based on medical knowledge and clinical experience.

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References

1. Goodman RA, Posner SF, Huang ES, Parekh AK, Koh HK. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. Preventing chronic disease. 2013;10:E66.
2. Hagen K, Zwart JA, Aamodt AH, Nilsen KB, Brathen G, Helde G, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. The journal of headache and pain. 2010;11(1):67-73.
3. Mundal I, Grawe RW, Bjorngaard JH, Linaker OM, Fors EA. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. BMC musculoskeletal disorders. 2014;15:213.
4. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. The American journal of medicine. 1999;107(5A):5S-11S.
5. Longstreth GF, Thompson WG, Chey WD, Houghton LA, Mearin F, Spiller RC. Functional bowel disorders. Gastroenterology. 2006;130(5):1480-91.
6. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. Gut. 2012;61(10):1390-7.
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
8. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. The British journal of psychiatry : the journal of mental science. 2001;179:540-4.
9. Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. Journal of psychosomatic research. 2002;52(2):69-77.
10. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. Journal of psychosomatic research. 1997;42(1):17-41.
11. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine; 2005.
12. Ewing JA. Detecting alcoholism. The CAGE questionnaire. Jama. 1984;252(14):1905-7.
13. Skogen JC, Overland S, Knudsen AK, Mykletun A. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. Addictive behaviors. 2011;36(4):302-7.
14. Tikkinen KA, Johnson TM, 2nd, Tammela TL, Sintonen H, Haukka J, Huhtala H, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. Eur Urol. 2010;57(3):488-96.
15. Sandvik H, Seim A, Vanvik A, Hunskaar S. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. Neurourology and urodynamics. 2000;19(2):137-45.
16. Barry MJ, Fowler FJ, Jr., O'Leary MP, Bruskewitz RC, Holtgrewe HL, Mebust WK, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. The Journal of urology. 1992;148(5):1549-57; discussion 64.
17. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11
18. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. The American journal of clinical nutrition. 2004;79(3):379-84.

KH Vinjerui. Joint multimorbidity and frailty: common and associated with occupational inequalities throughout adulthood in the cross-sectional observational HUNT3 Survey in Norway.

19. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Post TW, editor. Waltham, MA: UpToDate; 2018 Oct 1, 2016.
20. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, editor. 2009.

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Appendix C.

Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational class and joint multimorbidity and frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

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Two conditions of multimorbidity and one dimension of frailty.

Age, yr.	Occupational class	Female PR	95% CI	PD	95% CI	Men PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.01, 1.79)	0.05	(0.00, 0.09)	0.81	(0.55, 1.20)	-0.03	(-0.08, 0.03)
	Low	2.20	(1.73, 2.81)	0.17	(0.12, 0.21)	1.19	(0.86, 1.65)	0.03	(-0.02, 0.08)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.19, 1.55)	0.06	(0.04, 0.09)	1.04	(0.85, 1.27)	0.01	(-0.03, 0.04)
	Low	1.97	(1.75, 2.20)	0.17	(0.15, 0.20)	1.43	(1.22, 1.68)	0.07	(0.04, 0.10)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.22, 1.47)	0.07	(0.05, 0.09)	1.14	(0.99, 1.31)	0.03	(0.00, 0.05)
	Low	1.84	(1.70, 2.00)	0.17	(0.15, 0.19)	1.52	(1.35, 1.70)	0.09	(0.07, 0.12)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.21, 1.42)	0.07	(0.05, 0.09)	1.23	(1.11, 1.36)	0.04	(0.02, 0.07)
	Low	1.72	(1.60, 1.84)	0.17	(0.15, 0.19)	1.58	(1.44, 1.72)	0.11	(0.09, 0.13)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.27	(1.17, 1.37)	0.07	(0.05, 0.10)	1.29	(1.18, 1.41)	0.06	(0.04, 0.09)
	Low	1.59	(1.49, 1.70)	0.16	(0.14, 0.18)	1.60	(1.48, 1.73)	0.13	(0.11, 0.15)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(1.08, 1.25)	0.06	(0.03, 0.09)	1.35	(1.25, 1.46)	0.10	(0.08, 0.13)
	Low	1.37	(1.29, 1.46)	0.13	(0.11, 0.16)	1.56	(1.46, 1.68)	0.16	(0.14, 0.18)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.11	(1.03, 1.19)	0.04	(0.02, 0.07)	1.35	(1.26, 1.45)	0.11	(0.09, 0.14)
	Low	1.27	(1.20, 1.35)	0.11	(0.09, 0.14)	1.51	(1.41, 1.61)	0.17	(0.14, 0.19)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.05	(0.98, 1.14)	0.03	(-0.01, 0.06)	1.32	(1.24, 1.42)	0.12	(0.09, 0.15)
	Low	1.19	(1.11, 1.27)	0.09	(0.06, 0.12)	1.43	(1.35, 1.53)	0.16	(0.14, 0.19)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.01	(0.92, 1.10)	0.00	(-0.05, 0.05)	1.28	(1.19, 1.38)	0.12	(0.09, 0.16)
	Low	1.11	(1.03, 1.21)	0.06	(0.02, 0.10)	1.35	(1.25, 1.45)	0.15	(0.12, 0.19)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.17)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.93	(0.81, 1.06)	-0.05	(-0.14, 0.04)	1.17	(1.04, 1.32)	0.10	(0.03, 0.17)
	Low	1.00	(0.89, 1.13)	0.00	(-0.08, 0.08)	1.19	(1.06, 1.33)	0.11	(0.04, 0.18)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.90	(0.77, 1.05)	-0.07	(-0.18, 0.04)	1.12	(0.98, 1.29)	0.08	(-0.01, 0.17)
	Low	0.96	(0.85, 1.10)	-0.03	(-0.12, 0.07)	1.12	(0.98, 1.27)	0.08	(-0.01, 0.16)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.88	(0.74, 1.05)	-0.09	(-0.22, 0.03)	1.08	(0.93, 1.24)	0.06	(-0.05, 0.16)
	Low	0.94	(0.82, 1.08)	-0.05	(-0.15, 0.06)	1.06	(0.93, 1.22)	0.05	(-0.06, 0.15)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.86	(0.72, 1.04)	-0.11	(-0.25, 0.03)	1.04	(0.90, 1.20)	0.03	(-0.08, 0.15)
	Low	0.92	(0.80, 1.06)	-0.07	(-0.18, 0.05)	1.02	(0.89, 1.17)	0.02	(-0.09, 0.13)

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Three conditions of multimorbidity and two dimensions of frailty.

Age, yr.	Occupational class	Female				Men			
		PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.74	(1.60, 4.71)	0.04	(0.02, 0.06)	1.15	(0.57, 2.32)	0.01	(-0.02, 0.03)
	Low	4.24	(2.61, 6.89)	0.07	(0.05, 0.10)	1.36	(0.74, 2.51)	0.01	(-0.01, 0.04)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.98	(1.51, 2.59)	0.04	(0.03, 0.06)	1.41	(0.97, 2.05)	0.02	(0.00, 0.04)
	Low	3.06	(2.41, 3.90)	0.09	(0.07, 0.11)	1.81	(1.31, 2.50)	0.04	(0.02, 0.05)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.73	(1.43, 2.09)	0.04	(0.03, 0.06)	1.51	(1.16, 1.96)	0.03	(0.01, 0.04)
	Low	2.63	(2.23, 3.11)	0.10	(0.08, 0.11)	1.97	(1.57, 2.47)	0.05	(0.04, 0.07)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.55	(1.33, 1.79)	0.04	(0.03, 0.06)	1.58	(1.30, 1.91)	0.04	(0.02, 0.05)
	Low	2.29	(2.01, 2.60)	0.10	(0.09, 0.11)	2.07	(1.75, 2.44)	0.07	(0.05, 0.08)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.41	(1.23, 1.61)	0.04	(0.02, 0.06)	1.62	(1.38, 1.89)	0.05	(0.03, 0.06)
	Low	2.01	(1.78, 2.26)	0.10	(0.09, 0.11)	2.09	(1.82, 2.40)	0.08	(0.07, 0.09)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.07)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.24	(1.09, 1.41)	0.04	(0.01, 0.06)	1.59	(1.39, 1.83)	0.07	(0.05, 0.08)
	Low	1.60	(1.43, 1.79)	0.09	(0.07, 0.11)	1.94	(1.71, 2.20)	0.10	(0.09, 0.12)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(1.05, 1.35)	0.03	(0.01, 0.06)	1.54	(1.35, 1.75)	0.07	(0.05, 0.09)
	Low	1.45	(1.30, 1.62)	0.08	(0.06, 0.10)	1.79	(1.59, 2.01)	0.11	(0.09, 0.13)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(1.02, 1.34)	0.04	(0.01, 0.06)	1.46	(1.29, 1.65)	0.08	(0.05, 0.10)
	Low	1.33	(1.18, 1.50)	0.07	(0.04, 0.10)	1.61	(1.44, 1.80)	0.10	(0.08, 0.12)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(0.98, 1.37)	0.04	(0.00, 0.08)	1.36	(1.19, 1.56)	0.07	(0.04, 0.11)
	Low	1.23	(1.06, 1.44)	0.06	(0.02, 0.09)	1.41	(1.25, 1.60)	0.09	(0.06, 0.11)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(0.88, 1.61)	0.06	(-0.04, 0.15)	1.16	(0.92, 1.46)	0.05	(-0.03, 0.13)
	Low	1.09	(0.83, 1.44)	0.03	(-0.05, 0.11)	1.05	(0.83, 1.31)	0.01	(-0.06, 0.09)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.23	(0.83, 1.82)	0.07	(-0.06, 0.21)	1.06	(0.79, 1.43)	0.02	(-0.09, 0.14)
	Low	1.04	(0.72, 1.50)	0.01	(-0.10, 0.13)	0.89	(0.66, 1.19)	-0.04	(-0.15, 0.07)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.28	(0.77, 2.10)	0.09	(-0.09, 0.27)	0.97	(0.68, 1.40)	-0.01	(-0.18, 0.15)
	Low	1.00	(0.63, 1.59)	0.00	(-0.16, 0.16)	0.76	(0.53, 1.09)	-0.11	(-0.27, 0.04)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(0.72, 2.47)	0.12	(-0.12, 0.35)	0.90	(0.60, 1.36)	-0.05	(-0.27, 0.16)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			

Study design	#4	Present key elements of study design early in the paper	3-4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	3-4
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4 + appendix B
Bias	#9	Describe any efforts to address potential sources of bias	5
Study size	#10	Explain how the study size was arrived at	NA, data collected a priori, informal assesment
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	5
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	N/A

Statistical methods	#12e	Describe any sensitivity analyses	N/A
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	3-5, fig. 1
Participants	#13b	Give reasons for non-participation at each stage	Fig. 1
Participants	#13c	Consider use of a flow diagram	Fig. 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	5-6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	6, Tab. 2
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	4
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	We only gave adjusted estimates, p.6
Main results	#16b	Report category boundaries when continuous variables were categorized	6
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A, we used postestimation commands to obtain ratios and differences

Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	5, Appendix c
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	9
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	9
Generalisability	#21	Discuss the generalisability (external validity) of the study results	9
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

BMJ Open

Prevalence of multimorbidity with frailty and associations with socioeconomic position in an adult population: findings from the cross-sectional HUNT Study in Norway.

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Prevalence of multimorbidity with frailty and associations with socioeconomic position in an adult population: findings from the cross-sectional HUNT Study in Norway.

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Multimorbidity. Frailty. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: To explore prevalences and occupational group inequalities of two measures of multimorbidity with frailty.

Design: Cross-sectional study.

Setting: The Nord-Trøndelag Health Study (HUNT), Norway, a total county population health survey, 2006-2008.

Participants: Participants older than 25 years, with complete questionnaires, measurements and occupation data, were included.

Outcomes: ≥2 of 51 multimorbid conditions with ≥1 of 4 frailty measures (poor health, mental illness, physical impairment or social impairment) and ≥3 of 51 multimorbid conditions with ≥2 of 4 frailty measures.

Analysis: Logistic regression models with age and occupational group, were specified for each sex separately.

Results: Of 41193 adults, 38027 (55% women; 25-100 years old) were included. 39% had ≥2 multimorbid conditions with ≥1 frailty measure, and 17% had ≥3 multimorbid conditions with ≥2 frailty measures. Prevalence differences in percentage points of those in high vs low occupational group with ≥2 multimorbid conditions and ≥1 frailty measure, were 17 (95% CI,14 to 20) in women and 5 (1 to 9) in men at 30 years; 15 (13 to 17) in both sexes at 55 years; and 3 (-3 to 9) in women and 14 (9 to 18) in men at 80 years. In those with ≥3 multimorbid conditions and ≥2 frailty measures, prevalence differences were 8 (6 to 10) in women and 2 (0 to 4) in men at 30 years; 10 (8 to 11) in women and 9 (8 to 11) in men at 55 years, and 4 (-1 to 10) in women and 6 (1 to 10) in men at 80 years.

Conclusion: Multimorbidity with frailty is common and social inequalities persist until age 80 years in women and throughout the lifespan in men. To manage complex multimorbidity, strategies for proportionate universalism in medical education, health care, public health prevention and promotion seem necessary.

ARTICLE SUMMARY

Strengths and limitations of this study

1. The HUNT Study is a large total county population general health survey with a multitude of variables, suitable to estimate prevalences of multimorbidity and frailty by self-reports and clinical measurements.
2. Occupation is used as a marker for socioeconomic position, enabling international comparison.
3. Sex-specific occupational group differences in multimorbidity with frailty are reported as both absolute and relative measures of inequality
4. As a secondary analysis, the measures in this study need to be adjusted to fit previously collected data.
5. In particular, the original data lacked information of chronicity of conditions, which may lead to overestimation of multimorbidity.

INTRODUCTION

Multimorbidity, the co-occurrence of multiple, chronic conditions, where none is more central,[1] is increasingly prevalent and becoming the norm.[2-4] Multimorbidity is associated with high health care utilization[5] and challenges clinicians in a fragmented health care system, aided by single disease guidelines.[6] The treatment burden to patients is often substantial including lowered ability to self-care.[6] Ways to harmonize guidelines to fit multimorbidity[7 8] and manage patients with multimorbidity in clinical practice[6] have been explored, and specific multimorbidity care guidelines are emerging.[9 10]

Multimorbidity alone may not imply a need for complex, multidisciplinary care.[11] Sociodemographic characteristics, individual health and social experiences, and mental and somatic health characteristics,[12] increase patient complexity. The British National Institute for Health and Care Excellence (NICE) guideline,[10] defines multimorbidity as two or more long-term, single-count health conditions and recommends a multimorbid approach to care in various contexts, including mixed mental and somatic multimorbidity and multimorbidity with frailty.

Frailty is considered a dynamic state of multicausality, involving loss of function in spheres such as physical, psychological, and social domains and which increases vulnerability for adverse outcomes.[13] The NICE guideline proposes identification of frailty through observation of a low gait speed or poor self-rated health or by scoring a frailty scale combining demographic characteristics and multidimensional impairments.[14]

Social health inequalities are established; low socioeconomic position is associated with poorer health outcomes in Nordic countries[15] and globally.[16] Multimorbidity and frailty are no exception. Common determinants are socioeconomic deprivation,[17 18] female sex,[17 19] and higher age.[17 19] In descriptive studies, any indicator of socioeconomic position will detect occurring differences.[20] Socioeconomic gradients in prevalence of multimorbidity and frailty, has been explored by education,[17 18 21 22] income,[21 22] occupation,[3] and deprivation indexes.[17 18] Occupation is associated with education and income and may have an impact on health outcomes through biopsychosocial work exposures.[20] Although proportions with multimorbidity and frailty increase with higher age, more multimorbid are young and middle aged than old[4 23] and frailty is associated with multimorbidity and mortality from middle age.[24] The NICE guideline emphasizes assessment of a multimorbid approach to care for adults of all ages but does not take into account social position.

There are numerous operational definitions of both multimorbidity and frailty. The literature suggests that multimorbidity, defined as three or more single health conditions, increases specificity especially in older age groups.[25 26] Common frailty scales require multidimensional loss of function to identify frail individuals[19] and share ability to show associations to age, sex and mortality.[19]

The overall purpose of this study is to identify how many in a general adult population is likely to need complex, multidisciplinary care as given by one of the contexts suggested by the NICE guideline; multimorbidity with frailty. Two measures will be assessed, one in line with the guideline (two conditions of multimorbidity plus one dimension of frailty) and the other with expected increased specificity (three conditions of multimorbidity plus two dimensions of frailty). The second aim is to examine associations of these measures according to age, sex, and socioeconomic position.

MATERIALS AND METHODS

Reporting statement

The STROBE cross sectional reporting guidelines[27] were used for reporting of this observational study.

Study design and population

This cross-sectional study use data from the third wave in the Norwegian HUNT Study (the HUNT3 Survey, 2006-2008). Details on data collection and the cohort profile of this total county population health survey was published previously.[28] In brief, 93860 residents older than 20 years were invited. 54% (n=50807 of 93860) completed the main questionnaire, meeting the minimum requirement for HUNT3 Survey attendance.[28] Figure 1 presents the sample selection for this analysis.

81% (41193 of 50807) eligible participants completed all major parts of the HUNT3 Survey; the main, age- and sex-specific questionnaires; interviews; and measurements. Incomplete participation excluded 9610 individuals, while four missed complete information on participation. 1569 respondents were younger than 25 years and were excluded on the assumption that the highest level of occupational group may not yet be obtained by those in this age category. One missed information on age. 1571 individuals missed information on occupation, while 25 people had "unspecified occupation" and was excluded. 38027 of 41193 (92%) participants were included in the final sample.

Overall, lower socioeconomic position was associated with lower participation rate in the HUNT3 Survey.[29] In this study, the distribution of occupational groups was 24% (high), 27% (middle) and 49% (low) in the sample and 17% (high), 20% (middle), 52% (low) and 11% (missing) among non-eligible. 100% of the missing were due to missing classifiable occupational data. Women constituted 55%, 51% and 81%, of the sample, non-eligible and missing, respectively. The mean (standard deviation) age was 55 (14) years in the sample, 44 (18) years among non-eligible and 66 (18) years among those missing data.

Demographic and Sociodemographic Characteristics

Sex and age at participation in the HUNT3 Survey was constructed by the HUNT Databank. Occupational group was used as indicator of socioeconomic position.[20] In the HUNT3 Survey interview, all participants were asked, "What is/was the title of your main occupation?" Free-text answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,[30] which is based on the International Standard Classification of Occupations-88.[31] Occupational socioeconomic position was operationalized using occupation only, corresponding to a simplified version of the European Socio-economic Classification scheme.[32] The scheme aims to differentiate occupational groups on employment relationships and is not hierarchical per se. Still, the higher occupational groups are likely to have higher and more secure income.[32] Collapsed to a 3-class version, the high level represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and supervisory occupations. The middle group consist of small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The low level contains lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. Details are provided in appendix A.

Outcomes

Multimorbidity

The construction of 51 single, chronic conditions from the HUNT3 Survey data, is described in appendix B. Table 1 lists the 51 conditions by 14 ICD-10 chapters, a disease classification system in major organized by organ systems. In this study, a simple, non-weighted summary score was generated and two multimorbidity variables created, with cutoff values of at least 2 of 51 and 3 of 51 conditions.

Table 1. Conditions grouped by ICD-10 chapter.

ICD-10 chapter	Conditions
II	**Neoplasms**
	Cancer
III	**Blood/blood-forming organs/ immune mechanism**
	Sarcoidosis
IV	**Endocrine/nutritional/metabolic**
	Obesity
	Hypercholesterolemia
	Diabetes
	Hypothyroidism
	Hyperthyroidism
V	**Mental/behavioural**
	Alcohol problem
	Depression
	Anxiety
	Insomnia
VI	**Nervous system**
	Epilepsy
	Migraine
	Chronic headache, other
VII	**Eye/adnexa**
	Cataract
	Macula degeneration
	Glaucoma
VIII	**Ear/mastoid**
	Hearing impairment
IX	**Circulatory system**
	Undetected hypertension
	Angina pectoris
	Myocardial infarction
	Heart failure
	Other heart disease[1]
	Stroke or brain haemorrhage[1]
X	**Respiratory system**
	Chronic bronchitis, emphysema or COPD[1,2]
	Asthma
XI	**Digestive system**
	Dental health status
	Gastro-oesophageal reflux disease
	Irritable bowel syndrome
XII	**Skin/subcutaneous tissue**
	Hand eczema
	Psoriasis
XIII	**Musculoskeletal/connective tissue**
	Rheumatoid arthritis
	Osteoarthritis
	Ankylosing spondylitis
	Fibromyalgia
	Osteoporosis
	Local musculoskeletal pain/stiffness in:
	- Neck
	- Upper back
	- Lower back
	- Shoulder
	- Elbow
	- Hand
	- Hip
	- Knee
	- Foot/ancle
XIV	**Genitourinary system**
	Kidney disease
	Urine incontinence
	Prostate symptoms
	Menopausal hot flashes
XVIII	**Symptoms/signs/abnormal clinical/ laboratory findings**
	Nocturia
	Chronic widespread pain

[1] = Exception to single entity.

[2]COPD = Chronic Obstructive Pulmonary Disease.

Frailty

Original data did not match any exact frailty scale. Hence general, mental, physical and social dimensions[13 14 19] of frailty were operationalized from six original variables:

1. General health status, defined as those reporting the answers “poor” or “not so good” (vs “good” and “very good”) to the single question “How is your health at the moment?”
2. Mental health status, included those reporting symptoms of anxiety and/or depression, on the Hospital Anxiety and Depression Scale. The HUNT Databank calculated a total score for subscales of anxiety and depression, if all items for anxiety and depression, respectively, were answered. In this study, cutoff was set at 8/21 points for both conditions[33] and a combined variable was created.
3. Physical impairment was identified by combining those reporting “yes” (vs “no”) in response to the question, “Do you suffer from any long-term (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” and reporting either motor ability, vision, or hearing impairment to a moderate or severe degree.
4. Social impairment was derived from answers to the single question, “To what extent has your physical health or emotional problems limited you in your usual socializing with family or friends during the last 4 weeks?” Included were those reporting “much” and “not able to socialize” (vs “not at all,” “very little,” or “somewhat”).

A summary score was generated and two frailty variables created, with cutoff values of at least 1 of 4 and 2 of 4 frailty measures with impairment.

Multimorbidity with frailty

The two final outcome variables, were created by combining self-reported multimorbidity and frailty as at least 2 of 51 chronic health conditions plus impairment in 1 of 4 dimensions of frailty and 3 of 51 chronic health conditions plus impairments in 2 of 4 dimensions of frailty.

Statistical analysis

We used cross-tables to identify sociodemographic characteristics by occupational group (table 2) and by multimorbidity with frailty, stratified by sex (table 3).

Associations between occupational group and the two measures of multimorbidity with frailty were analyzed using logistic regression, adjusted for age and sex. All models were stratified by sex and included occupational group, continuous age, age squared, and an interaction term between occupational group and age. Likelihood ratio tests were used to compare models.

Given the high prevalence of multimorbidity with frailty and the knowledge that odds ratios will deviate from relative risks,[34] we used postestimation commands to obtain prevalence differences and prevalence ratios[35] between the occupational groups with high occupational group as the reference category. The prevalence difference is the difference in mean predicted probability, and prevalence ratio is the ratio between the mean predicted probabilities while holding other covariates constant.[35] Prevalence difference and prevalence

ratio between occupational groups were calculated at age 25 to 100 years in 5-year intervals (appendix C). Calculations (with 95% confidence intervals) are presented at the ages 30, 55 and 80 to reflect young adults, middle aged and elderly (table 4).

We performed complete case analysis and used Stata version 15.1 (StataCorp. College Station, TX, USA) to analyze the data.

Patient and public involvement

During the preparation of the HUNT3 Survey, there was a wide citizen and stakeholder participation. This study is a secondary analysis of data collected in 2006-2008. Multimorbidity is a universal topic, not represented by any particular patient group, thus no patient or public representative were involved in designing the study.

RESULTS

38027 individuals, older than 25 years, who had completed all major parts of the HUNT3 Survey and had data on occupation, comprised the final sample for this study (fig. 1). Further sociodemographic characteristics is presented in table 2.

Table 2. Sex and age distribution by occupational group.

	Occupational group							
	High		Middle		Low		Total	
	Frequency	(%)	Frequency	(%)	Frequency	(%)	Frequency	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Female	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
Male	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, years								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

The low occupational group is the largest overall, with 49% (n=18814 of 38027) of the sample. Furthermore, the low occupational group is the largest in absolute numbers in all age groups. There are more women (n=10922 of 18814 [58%]) than men (n=7892 of 18814 [42%]) in the low occupational group and in total with 20813 women (of 38027 [55%]) and 17214 men (of 38027 [45%]). The group aged 45 to 64 years constitutes the largest age group in all occupational groups and overall (n=18206 of 38027 [48%]).

Table 3. Frequency distribution of two definitions of multimorbidity with frailty across occupational groups and age categories, stratified by sex.

	Women						Men					
	Two conditions of multimorbidity and one dimension of frailty*						**Two conditions of multimorbidity and one dimension of frailty***					
	No, freq.	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**	**No, freq.**	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**
Total	12 304	(59)	8 482	(41)	20 813	(100)	10 826	(63)	6 378	(37)	17 214	(100)
Occupational group												
High	3 222	(72)	1 282	(28)	4 505	(100)	3 220	(72)	1 242	(28)	4 465	(100)
Middle	3 370	(63)	2 009	(37)	5 386	(100)	2 995	(62)	1 860	(38)	4 857	(100)
Low	5 712	(52)	5 191	(48)	10 922	(100)	4 611	(58)	3 276	(42)	7 892	(100)
Age, years												
25-44	4 298	(72)	1 680	(28)	5 981	(100)	3 075	(78)	867	(22)	3 943	(100)
45-64	5 712	(58)	4 122	(42)	9 840	(100)	5 398	(65)	2 967	(35)	8 366	(100)
65-74	1 615	(51)	1 548	(49)	3 168	(100)	1 681	(54)	1 409	(46)	3 093	(100)
75-100	679	(37)	1 132	(62)	1 824	(100)	672	(37)	1 135	(63)	1 812	(100)
Mean (SD)	52	(14)	58	(14)	54	(14)	54	(14)	61	(14)	56	(14)
	Three conditions of multimorbidity and two dimensions of frailty*						**Three conditions of multimorbidity and two dimensions of frailty***					
	No, freq.	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**	**No, freq.**	**(%)**	**Yes, freq.**	**(%)**	**Total, freq.**	**(%)**
Total	16 983	(82)	3 803	(18)	20 813	(100)	14 367	(83)	2 837	(16)	17 214	(100)
Occupational group												
High	4 029	(89)	475	(11)	4 505	(100)	3 977	(89)	485	(11)	4 465	(100)
Middle	4 491	(83)	888	(16)	5 386	(100)	3 995	(82)	860	(18)	4 857	(100)
Low	8 463	(77)	2 440	(22)	10 922	(100)	6 395	(81)	1 492	(19)	7 892	(100)
Age, years												
25-44	5 378	(90)	600	(10)	5 981	(100)	3 651	(93)	291	(7)	3 943	(100)
45-64	7 920	(80)	1 914	(19)	9 840	(100)	7 024	(84)	1 341	(16)	8 366	(100)
65-74	2 449	(77)	714	(23)	3 168	(100)	2 472	(80)	618	(20)	3 093	(100)
75-100	1 236	(68)	575	(32)	1 824	(100)	1 220	(67)	587	(32)	1 812	(100)
Mean (SD)	53	(14)	60	(14)	54	(14)	55	(14)	63	(13)	56	(14)

Abbreviations: freq., frequency; SD, standard deviation

*In total, 27 women and 10 men miss data on both measures of multimorbidity with frailty.

In total, 77% and 62% were identified with more than two and three conditions of multimorbidity alone, respectively. Further, 41% and 18% of all met the criteria for frailty only, impairments in more than one and two dimensions, respectively. Table 3 shows the distribution of the combined measures across occupational groups stratified by sex.

Overall, 39% met the criteria of having at least two conditions of multimorbidity with one dimension of frailty (41% of women, 37% of men) and 17% met the criteria of three-condition multimorbidity with two dimensions of frailty (18% of women, 16% of men).

Proportions of multimorbidity with frailty increased with lower occupational rank, for both definitions and in both sexes. The increase from high to low occupational group, for two-condition multimorbidity with one dimension of frailty, was 28% to 48% in women and 28% to 42% in men. Corresponding numbers for three-condition multimorbidity with two dimensions of frailty, were 11% to 22% in women and 11% to 19% in men. The absolute numbers with any definition of multimorbidity with frailty, were greater in the low occupational group, than any age group.

Proportions of joint multimorbidity with frailty increased with age in both sexes, regardless of definition. Two-condition multimorbidity with one dimension of frailty was reported by 28% of women and 22% of men 25- to 44-year-old, increasing to 62% of women and 63% of men 75- to 100-year-old. Equivalent numbers for three-condition multimorbidity with two dimensions of frailty were 10% of women and 7% of men, increasing to 32% in both sexes. In absolute numbers, most individuals with co-present multimorbidity and frailty were 45- to 64-year-old.

Table 4. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) between occupational groups and multimorbidity with frailty, stratified by sex.

		Women				Men			
Age, years	**Occupational group**	**Two conditions of multimorbidity and one dimension of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
55	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
80	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.18)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
Age, years	**Occupational group**	**Three conditions of multimorbidity and two dimensions of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
55	High	1.00		0.00		1.00		0.00	
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.08)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
80	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)

Table 4 shows prevalence differences and prevalence ratios for each definition of multimorbidity with frailty between occupational groups for women and men at the ages 30, 55, and 80 years.

Prevalence differences in percentage points (pp) for two-condition multimorbidity with one dimension of frailty between high and low occupational groups were; at 30 years, 17 (14 to 20) pp in women and 5 (1 to 9) pp in men; at 55 years, 15 (13 to 17) pp in both sexes, and at 80 years, 3 (-3 to 9) pp in women and 14 (9 to 18) pp in men.

Compared with the high occupational group, the prevalence ratio for the low occupational group for two-condition multimorbidity with one dimension of frailty, was; at 30 years, 2.09 (1.76 to 2.47) for women and 1.32 (1.04 to 1.67) for men; at 55 years, 1.48 (1.38 to 1.58) for women and 1.60 (1.48 to 1.72) for men, and at 80 years 1.05 (0.95 to 1.16) for women and 1.27 (1.15 to 1.39) for men.

Correspondingly, prevalence differences in percentage points between high and low occupational groups for three-condition multimorbidity with two dimensions of frailty, were; at 30 years, 8 (CI: 6 to 10) pp in women and 2 (CI: 0 to 4) pp in men; at 55 years, 10 (CI: 8 to 11) pp

in women and 9 (CI: 8 to 11) pp in men, and at 80 years, 4 (CI: -1 to 10) pp in women and 6 (CI: 1 to 10) pp in men.

Prevalence ratio, comparing the low occupational group with the highest occupational group for three-conditions multimorbidity with two conditions of frailty, was; at 30 years, 3.59 (1.43 to 5.08) for women and 1.60 (1.02 to 2.51) for men; at 55 years 1.78 (1.59 to 2.00) for women and 2.05 (1.80 to 2.33) for men, and finally at 80 years, 1.16 (0.94 to 1.42) for women and 1.22 (1.04 to 1.44) for men.

DISCUSSION

Main results

In this adult population health study, multimorbidity with frailty was common as 39% met the criteria of two-condition multimorbidity plus one dimension of frailty and 17% met the criteria of three-condition multimorbidity plus two dimensions of frailty. Proportions increased with lower occupational group, higher age and female sex from 25 to 74 years, but was common across age groups in both sexes. Occupational inequalities were consistent in both sexes until 80 years of age.

Comparison with existing literature

Investigating two measures of multimorbidity with frailty in one sample offers a unique direct comparison of occurrences and socioeconomic gradients. Lower overall prevalence for the stricter measure three-condition multimorbidity with two dimensions of frailty, is expected. Defining multimorbidity by three or more conditions differentiates into older age[25 26]. The joint measure multimorbidity and frailty, show the same tendency, as 62% of 75- to 100-year-olds met the criteria of at least two-condition multimorbidity with one dimension of frailty, while 32% reported three-condition multimorbidity with two dimensions of frailty. In line with individual studies on multimorbidity[4 23] and frailty[24], most individuals with co-present multimorbidity and frailty are younger than 64 years. A recent commentary[11] emphasized exploring multimorbidity guidelines and frailty as part of multimorbidity's complexity. Overlap of multimorbidity and frailty has been studied extensively,[36] but was beyond the scope of this study. Other researchers have focused on separating the concepts.[37] We have identified one study that evaluated the NICE guideline's recommendation to tailor multimorbidity approach of care in the context of polypharmacy on several outcomes,[38] however, none that have studied prevalence and social determinants of multimorbidity with frailty. Low social position,[17 18] older age,[17 19] and female sex[17 19] are known common determinants of multimorbidity and frailty. We therefore argue that the direction of the sociodemographic determinants in this study are as expected. The magnitudes of these gradients, however, have not been comparable with other studies.

Mechanisms to explain findings

The aggregation of ill health, multimorbidity and frailty included, in lower socioeconomic positions is explained by numerous theories. Overall, unequal distribution of power, income and resources, result in fundamental different conditions of daily life yielding inequalities in health.[16] With regards to occupation, several mechanisms can explain associations to health outcomes.

The higher occupational group is expected to have higher, more stable income,[32 39] more beneficial social networks,[39] and more autonomy and control[32 39] at work. Adverse working conditions such as exposure to toxic work environments[20] or demanding physical requirements[39] tend to cluster in lower occupational groups.[16] Persisting health inequalities in assumed egalitarian Nordic countries, is partly understood as mortality selection, where, given the well-developed health care and welfare systems, frail individuals survive, but likely end up in a low social position.[15] Further, smoking, overall morbidity and mortality decreases at a higher rate among higher than lower social groups.[15] In this study, the demographic age distribution explain the high number of 45- to 64-years old with co-present multimorbidity and frailty. Additionally, incidence of new conditions, is associated with count of conditions at baseline,[4] as well as age,[4] thus individuals in lower occupational groups may aggregate conditions faster. The bidirectional association of health and occupation, may explain higher occupational group prevalence ratios in younger individuals,[20] while lower ratios by increasing age are expected, since multimorbidity with frailty is more common[40] with advancing age. Finally, survival bias justifies diminishing occupational differences at age 80 years.

Strengths and limitations

Materials and methods meet the standards of studies on multimorbidity, frailty, and social health inequalities, strengthening this study. In multimorbidity studies, population-based health surveys are the most frequent study design,[41] and prevalence estimates from self-reports are justified when studying large samples.[25] Deriving the condition count multimorbidity measures from a complete list of single-entity conditions, is shown to yield proper prevalence estimates.[26] A multidimensional frailty measure agrees with an holistic, unrestricted on age, conceptual definition of frailty[13] and with common frailty scales, which share ability to show associations to age, sex and mortality.[19] In descriptive studies, any measure of socioeconomic position will reveal health inequalities, if such exists.[20] Occupation is an established marker for socioeconomic position,[20] in which this study had individual data classified to facilitate international comparison. Finally, socioeconomic differences are explored as both absolute and relative measures[15] and presented by sex.[17]

There are always limitations in secondary analysis of data collected a priori and not for the purpose of the current study. Measures of multimorbidity and frailty are also manifold, and operationalizations were adjusted to fit the available data. This challenges the external validity and comparability between studies, however, is sought reduced through transparency of morbidities included and construction of variables. A majority of included multimorbidity conditions do not contain information regarding duration. Thus, reported prevalence of multimorbidity may be overestimated and not represent true chronicity. It is recognized that frailty scales may differ in accuracy of detecting frailty in younger age groups,[10 19] however, frailty symptoms are of great clinical value regardless of age.[10 42] Frailty was measured solely as self-report, an approach that may underestimate overall prevalence[43] and overestimate proportion among women compared to men.[43] Lastly, in the HUNT3 Survey participants were asked for their “main” occupation, which is not necessarily the current or longest lasting occupation, more commonly studied.[39] Younger than middle-aged may to some extent be misclassified in the lower occupational group, which will underestimate social differences in health among younger subjects. Occupational data may obscure current social context,[39] and

underestimate socioeconomic inequalities. Thus, the study would have benefitted from exploring socioeconomic position with several indicactors,[44] such as individual education and income or a household measure.

Attendance in the HUNT3 Survey varied by age, sex, and social position,[29] still, the HUNT study is considered representative for Norway as a whole[45] and the cohort follows trends in health development in western high-income countries.[46-48] Depression hindered participation,[29] which may yield underestimation of both multimorbidity and frailty. An overall bias towards healthy elders is probable, since eligibility depended on attendance at a screening station.

Implications for clinical practice and policy makers

This study aimed to quantify the total prevalence of adults in the general population who might need complex, multidisciplinary care assessed as the joint measure multimorbidity with frailty. In a clinical context, the definition of at least three-condition multimorbidity with two dimensions of frailty to detect individuals for whom to initiate a multimorbid approach to care, seems more feasible. Despite acknowledgement of the association of multimorbidity and frailty with age, sex, and socioeconomic position, guidelines and interventions have yet to take this into account in assessment and management for multimorbidity.[49] Based on literature and reproduction of social gradients in our study, we suggest that clinicians consider evaluation of multimorbidity and frailty in younger age groups with social context in mind. Further research on implementation of the multimorbid approach to care model and mortality is needed before recommending changing inclusion criteria in a guideline. Since multimorbidity is becoming the norm, the organization of health care should reform to fit person-centred, coordinated, multidisciplinary care. To prevent cases of multimorbidity and frailty and minimize social discrepancies, both universal and targeted life cycle approaches seem necessary. Frailty is independently associated with mortality, adjusted for multimorbidity,[24] and is reversible.[50] Thus detection of frailty is relevant for both public health and clinical purposes.

Future research

Some forms of biases are possible for both multimorbidity, frailty and social position, and a careful interpretation of findings is warranted. However, multimorbidity with frailty is common in this general population and with occupational inequalities throughout adulthood, even with stricter definitions. This adds knowledge to the public health literature about the sociodemographic distribution of multimorbidity with frailty in younger age groups, as well as very old individuals. On this background, we recommend exploring the sociodemographic distribution of alternative measures on multimorbidity, including patterns, aiming to detect individuals suspected in high need of complex, multidisciplinary health care. Furthermore, such measurements can be compared as prognostic factors for health care utilization and mortality.

CONCLUSION

Multimorbidity with frailty are common from young adulthood onward, with consistent socioeconomic inequalities until 80 years old. Prevention will require a proportionate universal approach on social determinants of health throughout the entire life span. The crucial need for person-centered multimorbid approach to care that acknowledges social context, demands

reforms in health care organizational structure, medical education, and treatment. Further research on competing measures of high-need multimorbidity and the association of these factors with health care utilization and mortality should be explored by socioeconomic position, age and sex.

FIGURES

Figure 1: Flowchart for sample selection: inclusion and exclusion criteria and missing data.

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COMPETING INTERESTS

None declared.

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AUTHOR CONTRIBUTIONS

KHV, ERS and KD conceptualized the study and all authors contributed to its design. KHV has analysed the data under supervision of ERS and all authors have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by ERS, KD and PB. All authors have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

LICENSE STATEMENT

PATIENT CONSENT

Participation in all parts of the HUNT3 Survey was voluntary, and written informed consent was obtained from all participants.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Operationalizing socioeconomic position.

Appendix B: Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix C: Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational group and multimorbidity with frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

REFERENCES

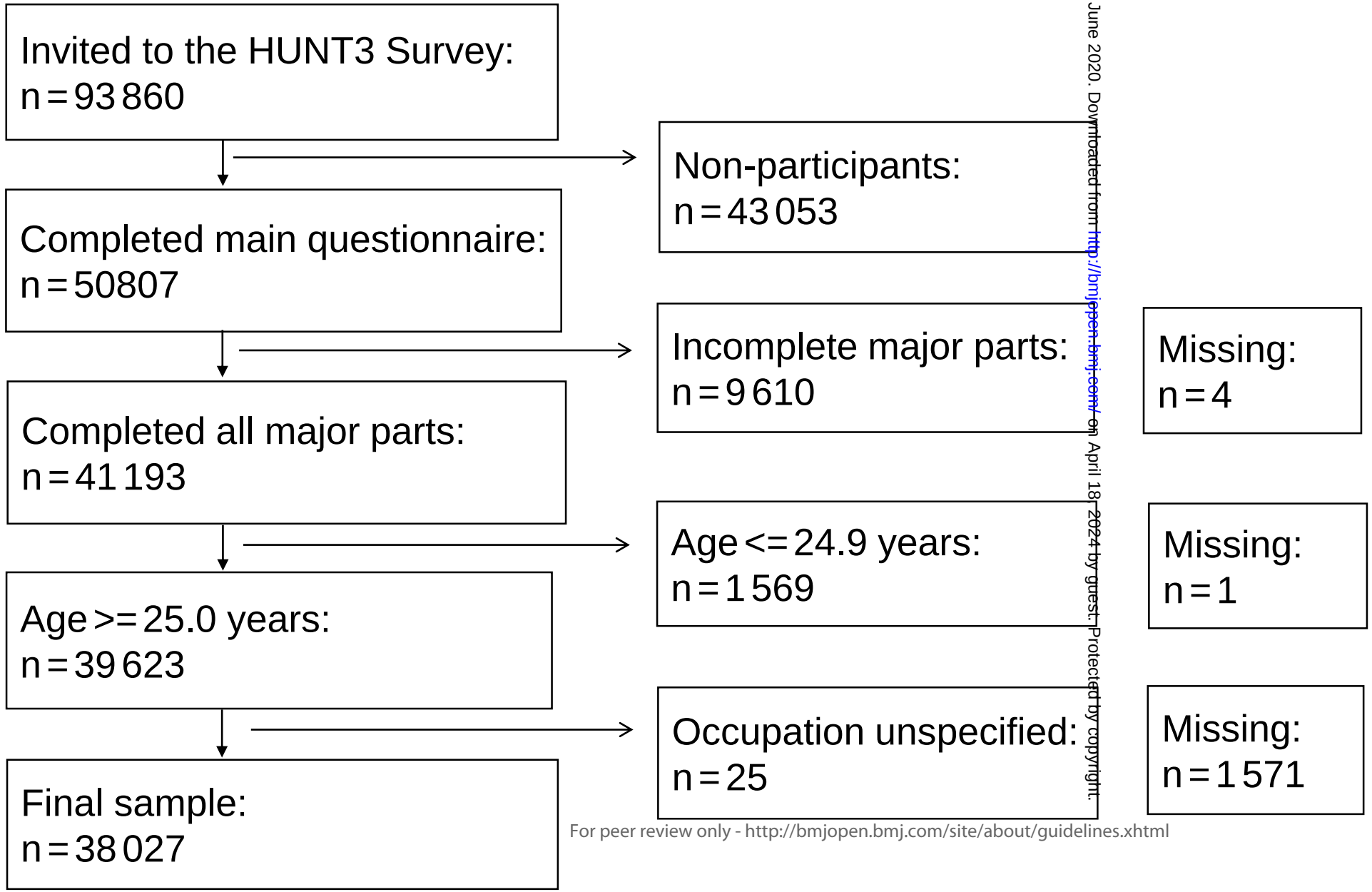
1. Boyd CM, Fortin M. Future of Multimorbidity Research: How Should Understanding of Multimorbidity Inform Health System Design? *Public Health Rev* 2010;32(2):451-74. doi: 10.1007/bf03391611
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLoS One* 2016;11(8):e0160264. doi: 10.1371/journal.pone.0160264 [published Online First: 2016/08/03]
3. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14 Suppl 1(sup1):28-32. doi: 10.1080/13814780802436093 [published Online First: 2008/10/31]
4. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 1998;51(5):367-75. doi: 10.1016/s0895-4356(97)00306-5 [published Online First: 1998/06/10]
5. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011;28(5):516-23. doi: 10.1093/fampra/cmr013 [published Online First: 2011/03/26]
6. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. *BMJ* 2015;350:h176. doi: 10.1136/bmj.h176 [published Online First: 2015/02/04]
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. *BMJ* 2012;345:e6341. doi: 10.1136/bmj.e6341 [published Online First: 2012/10/06]
8. Muth C, Kirchner H, van den Akker M, et al. Current guidelines poorly address multimorbidity: pilot of the interaction matrix method. *J Clin Epidemiol* 2014;67(11):1242-50. doi: 10.1016/j.jclinepi.2014.07.004 [published Online First: 2014/09/14]
9. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). *Health Policy* 2018;122(1):4-11. doi: 10.1016/j.healthpol.2017.09.006 [published Online First: 2017/10/03]
10. National Guideline C. Multimorbidity: clinical assessment and management. London: National Institute for Health and Care Excellence (UK). 2016.
11. Nicholson K, Makovski TT, Griffith LE, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. *J Clin Epidemiol* 2019;105:142-46. doi: 10.1016/j.jclinepi.2018.09.008 [published Online First: 2018/09/27]
12. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *Journal of comorbidity* 2012;2:1-9. doi: 10.15256/joc.2012.2.15 [published Online First: 2012/10/10]
13. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. In search of an integral conceptual definition of frailty: opinions of experts. *J Am Med Dir Assoc* 2010;11(5):338-43. doi: 10.1016/j.jamda.2009.09.015 [published Online First: 2010/06/01]
14. National Institute for Health and Care Excellence. Multimorbidity: clinical assessment and management. NICE guideline [NG56]. https://www.nice.org.uk/guidance/ng56: National Institute for Health and Care Excellence, 2016.
15. Huijts T, Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. *Eur J Public Health* 2009;19(5):452-3. doi: 10.1093/eurpub/ckp103 [published Online First: 2009/07/10]
16. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health. Geneva2008:9.

17. Violan C, Foguet-Boreu Q, Flores-Mateo G, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One* 2014;9(7):e102149. doi: 10.1371/journal.pone.0102149 [published Online First: 2014/07/23]
18. Franse CB, van Grieken A, Qin L, et al. Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One* 2017;12(11):e0187946. doi: 10.1371/journal.pone.0187946 [published Online First: 2017/11/10]
19. Theou O, Brothers TD, Pena FG, et al. Identifying common characteristics of frailty across seven scales. *J Am Geriatr Soc* 2014;62(5):901-6. doi: 10.1111/jgs.12773 [published Online First: 2014/04/05]
20. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull* 2007;81-82(1):21-37. doi: 10.1093/bmb/ldm001 [published Online First: 2007/02/08]
21. Agborsangaya CB, Lau D, Lahtinen M, et al. Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey. *BMC Public Health* 2012;12:201. doi: 10.1186/1471-2458-12-201 [published Online First: 2012/03/21]
22. Szanton SL, Seplaki CL, Thorpe RJ, Jr., et al. Socioeconomic status is associated with frailty: the Women's Health and Aging Studies. *J Epidemiol Community Health* 2010;64(1):63-7. doi: 10.1136/jech.2008.078428 [published Online First: 2009/08/21]
23. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2 [published Online First: 2012/05/15]
24. Hanlon P, Nicholl BI, Jani BD, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. *The Lancet Public Health* 2018;3(7):e323-e32. doi: 10.1016/s2468-2667(18)30091-4
25. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337 [published Online First: 2012/03/14]
26. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ Open* 2014;4(7):e004694. doi: 10.1136/bmjopen-2013-004694 [published Online First: 2014/07/13]
27. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014;12(12):1495-9. doi: 10.1016/j.ijsu.2014.07.013 [published Online First: 2014/07/22]
28. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. *Int J Epidemiol* 2013;42(4):968-77. doi: 10.1093/ije/dys095 [published Online First: 2012/08/11]
29. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012;12:143. doi: 10.1186/1471-2288-12-143 [published Online First: 2012/09/18]
30. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
31. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
32. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518
33. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
34. Sedgwick P. Relative risks versus odds ratios. *Bmj-British Medical Journal* 2014;348(feb07 2):g1407-g07. doi: ARTN g1407

10.1136/bmj.g1407
35. Norton EC, Miller MM, Kleinman LC. Computing Adjusted Risk Ratios and Risk Differences in Stata. *The Stata Journal: Promoting communications on statistics and Stata* 2018;13(3):492-509. doi: 10.1177/1536867x1301300304
36. Vetrano DL, Palmer K, Marengoni A, et al. Frailty and Multimorbidity: A Systematic Review and Meta-analysis. *J Gerontol A Biol Sci Med Sci* 2019;74(5):659-66. doi: 10.1093/gerona/gly110 [published Online First: 2018/05/05]
37. Fried LP, Ferrucci L, Darer J, et al. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;59(3):255-63. doi: 10.1093/gerona/59.3.m255 [published Online First: 2004/03/20]
38. Sasseville M, Smith SM, Freyne L, et al. Predicting poorer health outcomes in older community-dwelling patients with multimorbidity: prospective cohort study assessing the accuracy of different multimorbidity definitions. *BMJ Open* 2019;9(1):e023919. doi: 10.1136/bmjopen-2018-023919 [published Online First: 2019/01/07]
39. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12. doi: 10.1136/jech.2004.023531 [published Online First: 2005/12/20]
40. Scanlan JP. Guest Editorial. *Chance* 2013;19(2):47-51. doi: 10.1080/09332480.2006.10722787 [published Online First: 02 Aug 2013]
41. Willadsen TG, Bebe A, Koster-Rasmussen R, et al. The role of diseases, risk factors and symptoms in the definition of multimorbidity - a systematic review. *Scand J Prim Health Care* 2016;34(2):112-21. doi: 10.3109/02813432.2016.1153242 [published Online First: 2016/03/10]
42. Schuurmans H, Steverink N, Lindenberg S, et al. Old or frail: what tells us more? *J Gerontol A Biol Sci Med Sci* 2004;59(9):M962-5. doi: 10.1093/gerona/59.9.m962 [published Online First: 2004/10/09]
43. Theou O, O'Connell MD, King-Kallimanis BL, et al. Measuring frailty using self-report and test-based health measures. *Age Ageing* 2015;44(3):471-7. doi: 10.1093/ageing/afv010 [published Online First: 2015/02/18]
44. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. *JAMA* 2005;294(22):2879-88.
45. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk epidemiologi* 2003;13(1):19-32.
46. Collaboration NCDRF. Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature* 2019;569(7755):260-64. doi: 10.1038/s41586-019-1171-x [published Online First: 2019/05/10]
47. Collaboration NCDRF. Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017;389(10064):37-55. doi: 10.1016/S0140-6736(16)31919-5 [published Online First: 2016/11/20]
48. Collaboration NCDRF. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017;390(10113):2627-42. doi: 10.1016/S0140-6736(17)32129-3 [published Online First: 2017/10/17]
49. Smith SM, Soubhi H, Fortin M, et al. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *BMJ* 2012;345:e5205. doi: 10.1136/bmj.e5205 [published Online First: 2012/09/05]

50. Gill TM, Gahbauer EA, Allore HG, et al. Transitions between frailty states among community-living older persons. *Arch Intern Med* 2006;166(4):418-23. doi: 10.1001/archinte.166.4.418 [published Online First: 2006/03/01]

Fig. 1. Flowchart sample selection: inclusion and exclusion criteria and missing data.



Appendix A Operationalizing socioeconomic position using occupation.

In the HUNT3 Survey interview, all participants were asked: "What is/was the title of your main occupation?" Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,[1] which is based on the European Union's version of the *International Standard Classification of Occupations-88.*[2]

The standard categorize occupations according to skill level and specialization, degree of independence, and manual labor but not social position.[1] Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.[3] The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only[3], as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.[3]

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string "011" changed to numeric value "11," which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).[3]

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits).

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3 to 6, and “low” combining 7 to 9. [3] The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

Table A1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		**European Socio-economic**		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
3. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518

Appendix B

Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

ORIGINAL QUESTIONNAIRE, ENGLISH VERSION

Main questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

Sex- and age-specific questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

GENERAL COMMENTS

Chronicity

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care),[1] or 4: chronicity was assumed based on medical knowledge and clinical experience.

Missing

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

MAIN QUESTIONNAIRE

Hearing impairment

Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no. Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).

Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

"20 Diseases": Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis

Cluster text: "Have you had or do you have any of the following:
Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis?"
Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

Sex- and age-differentiated questionnaire

Headache

Seven questions in one block. Question 1: "Have you had headaches in the last year?" Yes/no.

Migraine without aura

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:

1. "What is the average strength of your headaches?" 1=Mild, 2=Moderate, 3=Strong.
   Recoded to dichotomous variable, where 1=Moderate/Strong.
2. "How long does the headache usually last?" 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days.
   Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
3. Cluster text: "Are the headaches usually characterized or accompanied by
   - Throbbing/thumping pain?" Yes, no.
   - Pain on one side of the head?" Yes, no.
   - Worsening with physical activity?" Yes, no.
   - Nausea and/or vomiting?" Yes, no.
   - Hypersensitivity to light and/or noise?" Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise).[2]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic headache

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:

1. "If yes (headache in the last year): What type of headache? Migraine, other."
   The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
2. "Average number of days a month with headaches:"
   1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days.
   Recoded to dichotomous variable, where 1= More than 14 days.

Included as case with chronic headache were those reporting "other" type of headache and an average frequency of more than 14 days per month.
Chronicity is assumed based on medical knowledge and clinical experience.

Pain

Index question: "In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?" Yes, no.
The follow-up question "If yes: Where have you had this pain or stiffness?" was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

Chronic widespread pain

Dichotomous variables were made for each major body area: 1) Trunk (neck, upper and lower back),
2) Upper limb (shoulder, elbow, hand), and 3) Lower limb (hip, knee, foot/ancle), where 1=At least one painful location. A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.[3]

Chronic, local pain

Of those who affirmed to pain or stiffness that has lasted more than three consecutive months,
chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

Thyroidal disease

Cluster text: "Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?" Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

Irritable bowel syndrome

Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:
“In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
“Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
“Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
“Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria.[4 5]

Gastro-oesophageal reflux disease

Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much). Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months.[6]

Anxiety

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered.
Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety.[8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Depression

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.
Depression was defined as HADS-D score >=8/21, indicating mild or possible depression.[8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic insomnia

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: “How often in the last 3 months have you
“Had difficulty falling asleep at night?” Never/seldom, sometimes, several times a week.
“Woken up repeatedly during the night?” Never/seldom, sometimes, several times a week.

"Woken too early and couldn't get back to sleep?" Never/seldom, sometimes, several times a week.
Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.[11]

Alcohol use disorder

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.12 The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.[13]
Chronicity is assumed based on medical knowledge and clinical experience.

Dental health problem

"How would you say your dental health is?" Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health.
Chronicity is assumed based on medical knowledge and clinical experience.

Menopausal hot flashes

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
"Do you have/have you had hot flashes due to menopause?" During the day, during the night, day and night, haven't had any.
"If you have had hot flashes, how would you describe them?" Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity.
Chronicity is assumed based on medical knowledge and clinical experience.

Nocturia

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.
"How many times do you get up during the night to urinate?" None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.[14]
Chronicity is assumed based on medical knowledge and clinical experience.

Urine incontinence

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.[15]
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. "If yes":

"How often do you have involuntary loss of urine?" Less than once a month, once or more per month, once or more per week, every day and/or night
"How much urine do you leak each time?" Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.[15]
Urine incontinence were included if severe to very severe.
Chronicity is assumed based on medical knowledge and clinical experience.

Prostate symptoms

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale [16] was slightly modified in HUNT3,[17] becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity, i.e. summary score >= 8 points.[16]
Chronicity is assumed based on medical knowledge and clinical experience.

Eye diseases

The age group 20-29 years were excluded.
Cluster text: "Do you have any of the following eye conditions?" Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.

Measurements

Obesity

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).18 19
Chronicity is assumed based on medical knowledge and clinical experience.

Hypertension

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.
Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures.
Chronicity is assumed based on medical knowledge and clinical experience.

Hypercholesterolemia

Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.[20]
Chronicity is assumed based on medical knowledge and clinical experience.

References

1. Goodman RA, Posner SF, Huang ES, et al. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66. doi: 10.5888/pcd10.120239 [published Online First: 2013/04/27]
2. Hagen K, Zwart JA, Aamodt AH, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. *J Headache Pain* 2010;11(1):67-73. doi: 10.1007/s10194-009-0174-7 [published Online First: 2009/12/01]
3. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. *BMC Musculoskelet Disord* 2014;15:213. doi: 10.1186/1471-2474-15-213 [published Online First: 2014/06/22]
4. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. *Am J Med* 1999;107(5A):5S-11S. doi: 10.1016/s0002-9343(99)00276-4 [published Online First: 1999/12/10]
5. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91. doi: 10.1053/j.gastro.2005.11.061 [published Online First: 2006/05/09]
6. Ness-Jensen E, Lindam A, Lagergren J, et al. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. *Gut* 2012;61(10):1390-7. doi: 10.1136/gutjnl-2011-300715 [published Online First: 2011/12/23]
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x [published Online First: 1983/06/01]
8. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry* 2001;179:540-4. doi: 10.1192/bjp.179.6.540 [published Online First: 2001/12/04]
9. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
10. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 1997;42(1):17-41. [published Online First: 1997/01/01]
11. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine 2005.
12. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905-7. doi: 10.1001/jama.252.14.1905 [published Online First: 1984/10/12]
13. Skogen JC, Overland S, Knudsen AK, et al. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. *Addict Behav* 2011;36(4):302-7. doi: 10.1016/j.addbeh.2010.11.010 [published Online First: 2010/12/21]
14. Tikkinen KA, Johnson TM, 2nd, Tammela TL, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol* 2010;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080 [published Online First: 2009/04/14]
15. Sandvik H, Seim A, Vanvik A, et al. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. *Neurourol Urodyn* 2000;19(2):137-45. [published Online First: 2000/02/19]
16. Barry MJ, Fowler FJ, Jr., O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549-57; discussion 64. doi: 10.1016/s0022-5347(17)36966-5 [published Online First: 1992/11/11]
17. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11 2019.
18. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79(3):379-84. doi: 10.1093/ajcn/79.3.379 [published Online First: 2004/02/27]
19. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Waltham, MA: UpToDate 2018.
20. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, ed., 2009.

Appendix C

Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational group and multimorbidity with frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

*Occup. = occupational.

Two conditions of multimorbidity and one dimension of frailty

Age,	Occup.*	Female				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.01, 1.79)	0.05	(0.00, 0.09)	0.81	(0.55, 1.20)	-0.03	(-0.08, 0.03)
	Low	2.20	(1.73, 2.81)	0.17	(0.12, 0.21)	1.19	(0.86, 1.65)	0.03	(-0.02, 0.08)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.19, 1.55)	0.06	(0.04, 0.09)	1.04	(0.85, 1.27)	0.01	(-0.03, 0.04)
	Low	1.97	(1.75, 2.20)	0.17	(0.15, 0.20)	1.43	(1.22, 1.68)	0.07	(0.04, 0.10)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.22, 1.47)	0.07	(0.05, 0.09)	1.14	(0.99, 1.31)	0.03	(0.00, 0.05)
	Low	1.84	(1.70, 2.00)	0.17	(0.15, 0.19)	1.52	(1.35, 1.70)	0.09	(0.07, 0.12)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.21, 1.42)	0.07	(0.05, 0.09)	1.23	(1.11, 1.36)	0.04	(0.02, 0.07)
	Low	1.72	(1.60, 1.84)	0.17	(0.15, 0.19)	1.58	(1.44, 1.72)	0.11	(0.09, 0.13)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.27	(1.17, 1.37)	0.07	(0.05, 0.10)	1.29	(1.18, 1.41)	0.06	(0.04, 0.09)
	Low	1.59	(1.49, 1.70)	0.16	(0.14, 0.18)	1.60	(1.48, 1.73)	0.13	(0.11, 0.15)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(1.08, 1.25)	0.06	(0.03, 0.09)	1.35	(1.25, 1.46)	0.10	(0.08, 0.13)
	Low	1.37	(1.29, 1.46)	0.13	(0.11, 0.16)	1.56	(1.46, 1.68)	0.16	(0.14, 0.18)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.11	(1.03, 1.19)	0.04	(0.02, 0.07)	1.35	(1.26, 1.45)	0.11	(0.09, 0.14)
	Low	1.27	(1.20, 1.35)	0.11	(0.09, 0.14)	1.51	(1.41, 1.61)	0.17	(0.14, 0.19)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.05	(0.98, 1.14)	0.03	(-0.01, 0.06)	1.32	(1.24, 1.42)	0.12	(0.09, 0.15)
	Low	1.19	(1.11, 1.27)	0.09	(0.06, 0.12)	1.43	(1.35, 1.53)	0.16	(0.14, 0.19)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.01	(0.92, 1.10)	0.00	(-0.05, 0.05)	1.28	(1.19, 1.38)	0.12	(0.09, 0.16)
	Low	1.11	(1.03, 1.21)	0.06	(0.02, 0.10)	1.35	(1.25, 1.45)	0.15	(0.12, 0.19)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.17)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.93	(0.81, 1.06)	-0.05	(-0.14, 0.04)	1.17	(1.04, 1.32)	0.10	(0.03, 0.17)
	Low	1.00	(0.89, 1.13)	0.00	(-0.08, 0.08)	1.19	(1.06, 1.33)	0.11	(0.04, 0.18)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.90	(0.77, 1.05)	-0.07	(-0.18, 0.04)	1.12	(0.98, 1.29)	0.08	(-0.01, 0.17)
	Low	0.96	(0.85, 1.10)	-0.03	(-0.12, 0.07)	1.12	(0.98, 1.27)	0.08	(-0.01, 0.16)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.88	(0.74, 1.05)	-0.09	(-0.22, 0.03)	1.08	(0.93, 1.24)	0.06	(-0.05, 0.16)
	Low	0.94	(0.82, 1.08)	-0.05	(-0.15, 0.06)	1.06	(0.93, 1.22)	0.05	(-0.06, 0.15)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.86	(0.72, 1.04)	-0.11	(-0.25, 0.03)	1.04	(0.90, 1.20)	0.03	(-0.08, 0.15)
	Low	0.92	(0.80, 1.06)	-0.07	(-0.18, 0.05)	1.02	(0.89, 1.17)	0.02	(-0.09, 0.13)

Three conditions of multimorbidity and two dimensions of frailty

Age,	Occup.*	Female				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.74	(1.60, 4.71)	0.04	(0.02, 0.06)	1.15	(0.57, 2.32)	0.01	(-0.02, 0.03)
	Low	4.24	(2.61, 6.89)	0.07	(0.05, 0.10)	1.36	(0.74, 2.51)	0.01	(-0.01, 0.04)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.98	(1.51, 2.59)	0.04	(0.03, 0.06)	1.41	(0.97, 2.05)	0.02	(0.00, 0.04)
	Low	3.06	(2.41, 3.90)	0.09	(0.07, 0.11)	1.81	(1.31, 2.50)	0.04	(0.02, 0.05)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.73	(1.43, 2.09)	0.04	(0.03, 0.06)	1.51	(1.16, 1.96)	0.03	(0.01, 0.04)
	Low	2.63	(2.23, 3.11)	0.10	(0.08, 0.11)	1.97	(1.57, 2.47)	0.05	(0.04, 0.07)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.55	(1.33, 1.79)	0.04	(0.03, 0.06)	1.58	(1.30, 1.91)	0.04	(0.02, 0.05)
	Low	2.29	(2.01, 2.60)	0.10	(0.09, 0.11)	2.07	(1.75, 2.44)	0.07	(0.05, 0.08)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.41	(1.23, 1.61)	0.04	(0.02, 0.06)	1.62	(1.38, 1.89)	0.05	(0.03, 0.06)
	Low	2.01	(1.78, 2.26)	0.10	(0.09, 0.11)	2.09	(1.82, 2.40)	0.08	(0.07, 0.09)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.07)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.24	(1.09, 1.41)	0.04	(0.01, 0.06)	1.59	(1.39, 1.83)	0.07	(0.05, 0.08)
	Low	1.60	(1.43, 1.79)	0.09	(0.07, 0.11)	1.94	(1.71, 2.20)	0.10	(0.09, 0.12)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(1.05, 1.35)	0.03	(0.01, 0.06)	1.54	(1.35, 1.75)	0.07	(0.05, 0.09)
	Low	1.45	(1.30, 1.62)	0.08	(0.06, 0.10)	1.79	(1.59, 2.01)	0.11	(0.09, 0.13)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(1.02, 1.34)	0.04	(0.01, 0.06)	1.46	(1.29, 1.65)	0.08	(0.05, 0.10)
	Low	1.33	(1.18, 1.50)	0.07	(0.04, 0.10)	1.61	(1.44, 1.80)	0.10	(0.08, 0.12)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(0.98, 1.37)	0.04	(0.00, 0.08)	1.36	(1.19, 1.56)	0.07	(0.04, 0.11)
	Low	1.23	(1.06, 1.44)	0.06	(0.02, 0.09)	1.41	(1.25, 1.60)	0.09	(0.06, 0.11)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(0.88, 1.61)	0.06	(-0.04, 0.15)	1.16	(0.92, 1.46)	0.05	(-0.03, 0.13)
	Low	1.09	(0.83, 1.44)	0.03	(-0.05, 0.11)	1.05	(0.83, 1.31)	0.01	(-0.06, 0.09)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.23	(0.83, 1.82)	0.07	(-0.06, 0.21)	1.06	(0.79, 1.43)	0.02	(-0.09, 0.14)
	Low	1.04	(0.72, 1.50)	0.01	(-0.10, 0.13)	0.89	(0.66, 1.19)	-0.04	(-0.15, 0.07)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.28	(0.77, 2.10)	0.09	(-0.09, 0.27)	0.97	(0.68, 1.40)	-0.01	(-0.18, 0.15)
	Low	1.00	(0.63, 1.59)	0.00	(-0.16, 0.16)	0.76	(0.53, 1.09)	-0.11	(-0.27, 0.04)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(0.72, 2.47)	0.12	(-0.12, 0.35)	0.90	(0.60, 1.36)	-0.05	(-0.27, 0.16)
	Low	0.96	(0.54, 1.73)	-0.01	(-0.22, 0.19)	0.65	(0.42, 0.99)	-0.19	(-0.39, 0.01)

Reporting checklist for cross sectional study.

Based on the STROBE cross sectional guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

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		Reporting Item	Page Number
Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			

Study design	#4	Present key elements of study design early in the paper	3-4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	3-4
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4 + appendix B
Bias	#9	Describe any efforts to address potential sources of bias	5
Study size	#10	Explain how the study size was arrived at	NA, data collected a priori, informal assesment
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	5
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	N/A

Statistical methods	#12e	Describe any sensitivity analyses	N/A
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	3-5, fig. 1
Participants	#13b	Give reasons for non-participation at each stage	Fig. 1
Participants	#13c	Consider use of a flow diagram	Fig. 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	5-6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	6, Tab. 2
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	4
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	We only gave adjusted estimates, p.6
Main results	#16b	Report category boundaries when continuous variables were categorized	6
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A, we used postestimation commands to obtain ratios and differences

Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	5, Appendix c
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	9
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	9
Generalisability	#21	Discuss the generalisability (external validity) of the study results	9
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10

BMJ Open

Prevalence of Multimorbidity with Frailty and Associations with Socioeconomic Position in an Adult Population: Findings from the Cross-sectional HUNT Study in Norway.

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Prevalence of Multimorbidity with Frailty and Associations with Socioeconomic Position in an Adult Population: Findings from the Cross-sectional HUNT Study in Norway

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Multimorbidity. Frailty. Socioeconomic status. Occupations. Public health. Health inequality. The HUNT Study.

ABSTRACT

Objectives: To explore prevalences and occupational group inequalities of two measures of multimorbidity with frailty.

Design: Cross-sectional study.

Setting: The Nord-Trøndelag Health Study (HUNT), Norway, a total county population health survey, 2006-2008.

Participants: Participants older than 25 years, with complete questionnaires, measurements and occupation data, were included.

Outcomes: ≥2 of 51 multimorbid conditions with ≥1 of 4 frailty measures (poor health, mental illness, physical impairment or social impairment) and ≥3 of 51 multimorbid conditions with ≥2 of 4 frailty measures.

Analysis: Logistic regression models with age and occupational group, were specified for each sex separately.

Results: Of 41193 adults, 38027 (55% women; 25-100 years old) were included. 39% had ≥2 multimorbid conditions with ≥1 frailty measure, and 17% had ≥3 multimorbid conditions with ≥2 frailty measures. Prevalence differences in percentage points of those in high vs low occupational group with ≥2 multimorbid conditions and ≥1 frailty measure, were 17 (95% CI,14 to 20) in women and 5 (1 to 9) in men at 30 years; 15 (13 to 17) in both sexes at 55 years; and 3 (-3 to 9) in women and 14 (9 to 18) in men at 80 years. In those with ≥3 multimorbid conditions and ≥2 frailty measures, prevalence differences were 8 (6 to 10) in women and 2 (0 to 4) in men at 30 years; 10 (8 to 11) in women and 9 (8 to 11) in men at 55 years, and 4 (-1 to 10) in women and 6 (1 to 10) in men at 80 years.

Conclusion: Multimorbidity with frailty is common and social inequalities persist until age 80 years in women and throughout the lifespan in men. To manage complex multimorbidity, strategies for proportionate universalism in medical education, health care, public health prevention and promotion seem necessary.

ARTICLE SUMMARY

Strengths and limitations of this study

1. The HUNT Study is a large total county population general health survey with a multitude of variables, suitable to estimate prevalences of multimorbidity and frailty by self-reports and clinical measurements.
2. Occupation is used as a marker for socioeconomic position, enabling international comparison.
3. Sex-specific occupational group differences in multimorbidity with frailty are reported as both absolute and relative measures of inequality
4. As a secondary analysis, the measures in this study need to be adjusted to fit previously collected data.
5. In particular, the original data lacked information of chronicity of conditions, which may lead to overestimation of multimorbidity.

INTRODUCTION

Multimorbidity, the co-occurrence of multiple, chronic conditions, where none is more central,[1] is increasingly prevalent and becoming the norm.[2-4] Multimorbidity is associated with high health care utilization[5] and challenges clinicians in a fragmented health care system, aided by single disease guidelines.[6] The treatment burden to patients is often substantial including lowered ability to self-care.[6] Ways to harmonize guidelines to fit multimorbidity[7 8] and manage patients with multimorbidity in clinical practice[6] have been explored, and specific multimorbidity care guidelines are emerging.[9 10]

Multimorbidity alone may not imply a need for complex, multidisciplinary care.[1] Sociodemographic characteristics, individual health and social experiences, and mental and somatic health characteristics,[11] increase patient complexity. The British National Institute for Health and Care Excellence (NICE) guideline,[10] defines multimorbidity as two or more long-term, single-count health conditions and recommends a multimorbid approach to care in various contexts, including mixed mental and somatic multimorbidity and multimorbidity with frailty.

Frailty increases the vulnerability for adverse outcomes. It has been understood as characterized by loss of biophysical reserves in elderly,[12] operationalized as the frailty phenotype.[12] Another approach is the frailty index,[13] which calculate a ratio of accumulation of numerous deficits in several domains. An opinion of experts, further emphasize the latter multidimensional view and defines frailty as a dynamic state of multicausality, involving loss of function in spheres such as physical, psychological, and social domains.[14] This can be regarded as a biopsychosocial frailty model.[15]The NICE guideline proposes identification of frailty through observation of a low gait speed or poor self-rated health or by scoring a frailty scale combining demographic characteristics and multidimensional impairments.[10]

Social health inequalities are established; low socioeconomic position is associated with poorer health outcomes in Nordic countries[16] and globally.[17] Multimorbidity and frailty are no exception. Common determinants are socioeconomic deprivation,[18 19] female sex,[18 20] and higher age.[18 20] In descriptive studies, any indicator of socioeconomic position will detect occurring differences.[21] Socioeconomic gradients in prevalence of multimorbidity and frailty, has been explored by education,[18 19 22 23] income,[22 23] occupation,[3] and deprivation indexes.[18 19] Occupation is associated with education and income and may have an impact on health outcomes through biopsychosocial work exposures.[21] Although proportions with multimorbidity and frailty increase with higher age, more multimorbid are young and middle aged than old[4 24] and frailty is associated with multimorbidity and mortality from middle age.[25] The NICE guideline emphasizes assessment of a multimorbid approach to care for adults of all ages but does not take into account social position.

There are numerous operational definitions of both multimorbidity and frailty and prevalence vary by setting, definitions and methods.[18 26-28] The literature suggests that multimorbidity, defined as three or more single health conditions, increases specificity especially in older age groups.[26 29] Common frailty scales require multidimensional loss of function to identify frail individuals[20] and share ability to show associations to age, sex and mortality.[20]

The overall purpose of this study is to identify how many in a general adult population is likely to need complex, multidisciplinary care as given by one of the contexts suggested by the NICE guideline; multimorbidity with frailty. Two measures will be assessed, one in line

with the guideline (two conditions of multimorbidity plus one dimension of frailty) and the other with expected increased specificity (three conditions of multimorbidity plus two dimensions of frailty). The second aim is to examine associations of these measures according to age, sex, and socioeconomic position.

MATERIALS AND METHODS

Reporting statement

The STROBE cross sectional reporting guidelines[30] were used for reporting of this observational study.

Study design and population

This cross-sectional study use data from the third wave in the Norwegian HUNT Study (the HUNT3 Survey, 2006-2008). Details on data collection and the cohort profile of this total county population health survey was published previously.[31] In brief, 93860 residents older than 20 years were invited. 54% (n=50807 of 93860) completed the main questionnaire, meeting the minimum requirement for HUNT3 Survey attendance.[31] Figure 1 presents the sample selection for this analysis.

81% (41193 of 50807) eligible participants completed all major parts of the HUNT3 Survey; the main, age- and sex-specific questionnaires; interviews; and measurements. Incomplete participation excluded 9610 individuals, while four missed complete information on participation. 1569 respondents were younger than 25 years and were excluded on the assumption that the highest level of occupational group may not yet be obtained by those in this age category. One missed information on age. 1571 individuals missed information on occupation, while 25 people had “unspecified occupation” and was excluded. 38027 of 41193 (92%) participants were included in the final sample.

Overall, lower socioeconomic position was associated with lower participation rate in the HUNT3 Survey.[32] In this study, the distribution of occupational groups was 24% (high), 27% (middle) and 49% (low) in the sample and 17% (high), 20% (middle), 52% (low) and 11% (missing) among non-eligible. 100% of the missing were due to missing classifiable occupational data. Women constituted 55%, 51% and 81%, of the sample, non-eligible and missing, respectively. The mean (standard deviation) age was 55 (14) years in the sample, 44 (18) years among non-eligible and 66 (18) years among those missing data.

Demographic and Sociodemographic Characteristics

Sex and age at participation in the HUNT3 Survey was constructed by the HUNT Databank. Occupational group was used as indicator of socioeconomic position.[21] In the HUNT3 Survey interview, all participants were asked, “What is/was the title of your main occupation?” Free-text answers were manually categorized corresponding to Standard Classifications of Occupations by Statistics Norway,[33] which is based on the International Standard Classification of Occupations-88.[34] Occupational socioeconomic position was operationalized using occupation only, corresponding to a simplified version of the European Socio-economic Classification scheme.[35] The scheme aims to differentiate occupational groups on employment relationships and is not hierarchical per se. Still, the higher occupational groups are likely to have higher and more secure income.[35] Collapsed to a 3-class version, the high level represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, and higher-grade technician and

supervisory occupations. The middle group consist of small employers, self-employed individuals, and lower-grade supervisory and technician occupations. The low level contains lower-grade service positions, sales and clerical occupations, and lower-grade technical and routine occupations. Details are provided in appendix A.

Outcomes

Multimorbidity

The construction of 51 single, chronic conditions from the HUNT3 Survey data, is described in appendix B. Table 1 lists the 51 conditions by 14 ICD-10 chapters, a disease classification system in major organized by organ systems. In this study, a simple, non-weighted summary score was generated and two multimorbidity variables created, with cutoff values of at least 2 of 51 and 3 of 51 conditions.

Table 1. Conditions grouped by ICD-10 chapter.

ICD-10 chapter	Conditions
II	**Neoplasms**
	Cancer
III	**Blood/blood-forming organs/ immune mechanism**
	Sarcoidosis
IV	**Endocrine/nutritional/metabolic**
	Obesity
	Hypercholesterolemia
	Diabetes
	Hypothyroidism
	Hyperthyroidism
V	**Mental/behavioural**
	Alcohol problem
	Depression
	Anxiety
	Insomnia
VI	**Nervous system**
	Epilepsy
	Migraine
	Chronic headache, other
VII	**Eye/adnexa**
	Cataract
	Macula degeneration
	Glaucoma
VIII	**Ear/mastoid**
	Hearing impairment
IX	**Circulatory system**
	Hypertension
	Angina pectoris
	Myocardial infarction
	Heart failure
	Other heart disease[1]
	Stroke or brain haemorrhage[1]
X	**Respiratory system**
	Chronic bronchitis, emphysema or COPD[1,2]
	Asthma
XI	**Digestive system**
	Dental health status
	Gastro-oesophageal reflux disease
	Irritable bowel syndrome
XII	**Skin/subcutaneous tissue**
	Hand eczema
	Psoriasis
XIII	**Musculoskeletal/connective tissue**
	Rheumatoid arthritis
	Osteoarthritis
	Ankylosing spondylitis
	Fibromyalgia
	Osteoporosis
	Local musculoskeletal pain/stiffness in:
	- Neck
	- Upper back
	- Lower back
	- Shoulder
	- Elbow
	- Hand
	- Hip
	- Knee
	- Foot/ancle
XIV	**Genitourinary system**
	Kidney disease
	Urine incontinence
	Prostate symptoms
	Menopausal hot flashes
XVIII	**Symptoms/signs/abnormal clinical/ laboratory findings**
	Nocturia
	Chronic widespread pain

[1] = Exception to single entity.

[2]COPD = Chronic Obstructive Pulmonary Disease.

Frailty

Original data did not match any exact frailty scale. A qualitative judgement of available data was undertaken and general, mental, physical and social dimensions[10 14 20] of frailty were operationalized from six original variables:

1. General health status, defined as those reporting the answers “poor” or “not so good” (vs “good” and “very good”) to the single question “How is your health at the moment?”
2. Mental health status, included those reporting symptoms of anxiety and/or depression, on the Hospital Anxiety and Depression Scale. The HUNT Databank calculated a total score for subscales of anxiety and depression, if all items for anxiety and depression, respectively, were answered. In this study, cutoff was set at 8/21 points for both conditions[36] and a combined variable was created.
3. Physical impairment was identified by combining those reporting “yes” (vs “no”) in response to the question, “Do you suffer from any long-term (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” and reporting either motor ability, vision, or hearing impairment to a moderate or severe degree.
4. Social impairment was derived from answers to the single question, “To what extent has your physical health or emotional problems limited you in your usual socializing with family or friends during the last 4 weeks?” Included were those reporting “much” and “not able to socialize” (vs “not at all,” “very little,” or “somewhat”).

A summary score was generated and two frailty variables created, with cutoff values of at least 1 of 4 and 2 of 4 frailty measures with impairment.

Multimorbidity with frailty

The two final outcome variables, were created by combining self-reported multimorbidity and frailty as at least 2 of 51 chronic health conditions plus impairment in 1 of 4 dimensions of frailty and 3 of 51 chronic health conditions plus impairments in 2 of 4 dimensions of frailty.

Statistical analysis

We used cross-tables to identify sociodemographic characteristics by occupational group (table 2) and by multimorbidity with frailty, stratified by sex (table 3).

Associations between occupational group and the two measures of multimorbidity with frailty were analyzed using logistic regression, adjusted for age and sex. All models were stratified by sex and included occupational group, continuous age, age squared, and an interaction term between occupational group and age. Likelihood ratio tests were used to compare models.

Given the high prevalence of multimorbidity with frailty and the knowledge that odds ratios will deviate from relative risks,[37] we used postestimation commands to obtain prevalence differences and prevalence ratios[38] between the occupational groups with high occupational group as the reference category. The prevalence difference is the difference in mean predicted probability, and prevalence ratio is the ratio between the mean predicted probabilities while holding other covariates constant.[38] Prevalence difference and prevalence ratio between occupational groups were calculated at age 25 to 100 years in 5-year intervals (appendix C). Calculations (with 95% confidence intervals) are presented at the ages 30, 55 and 80 to reflect young adults, middle aged and elderly (table 4).

We performed complete case analysis and used Stata version 15.1 (StataCorp. College Station, TX, USA) to analyze the data.

Patient and public involvement

During the preparation of the HUNT3 Survey, there was a wide citizen and stakeholder participation. This study is a secondary analysis of data collected in 2006-2008. Multimorbidity is a universal topic, not represented by any particular patient group, thus no patient or public representative were involved in designing the study.

RESULTS

38027 individuals, older than 25 years, who had completed all major parts of the HUNT3 Survey and had data on occupation, comprised the final sample for this study (fig. 1). Further sociodemographic characteristics is presented in table 2.

Table 2. Sex and age distribution by occupational group.

	Occupational group							
	High		Middle		Low		Total	
	Frequency	(%)	Frequency	(%)	Frequency	(%)	Frequency	(%)
Total	8 970	(100)	10 243	(100)	18 814	(100)	38 027	(100)
Sex								
Female	4 505	(50)	5 386	(53)	10 922	(58)	20 813	(55)
Male	4 465	(50)	4 857	(47)	7 892	(42)	17 214	(45)
Age, years								
25-44	2 837	(32)	2 600	(25)	4 487	(24)	9 924	(26)
45-64	4 468	(50)	4 787	(47)	8 951	(48)	18 206	(48)
65-74	1 118	(12)	1 846	(18)	3 297	(18)	6 261	(16)
75-100	547	(6)	1 010	(10)	2 079	(11)	3 636	(10)

Most participants, 49% (n=18814 of 38027), are categorized as low occupational group, which is comprised of 58% (n=10922 of 18814) women, while women constitute 55% (n=20813 of 38027) of the total sample.

Table 3. Frequency distribution of two definitions of multimorbidity with frailty across occupational groups and age categories, stratified by sex.

		Women						Men					
		Two conditions of multimorbidity and one dimension of frailty*						Two conditions of multimorbidity and one dimension of frailty*					
		No, freq.	(%)	Yes, freq.	(%)	Total, freq.	(%)	No, freq.	(%)	Yes, freq.	(%)	Total, freq.	(%)
Total		12 304	(59)	8 482	(41)	20 813	(100)	10 826	(63)	6 378	(37)	17 214	(100)
Occupational group													
	High	3 222	(72)	1 282	(28)	4 505	(100)	3 220	(72)	1 242	(28)	4 465	(100)
	Middle	3 370	(63)	2 009	(37)	5 386	(100)	2 995	(62)	1 860	(38)	4 857	(100)
	Low	5 712	(52)	5 191	(48)	10 922	(100)	4 611	(58)	3 276	(42)	7 892	(100)
Age, years													
	25-44	4 298	(72)	1 680	(28)	5 981	(100)	3 075	(78)	867	(22)	3 943	(100)
	45-64	5 712	(58)	4 122	(42)	9 840	(100)	5 398	(65)	2 967	(35)	8 366	(100)
	65-74	1 615	(51)	1 548	(49)	3 168	(100)	1 681	(54)	1 409	(46)	3 093	(100)
	75-100	679	(37)	1 132	(62)	1 824	(100)	672	(37)	1 135	(63)	1 812	(100)
Mean (SD)		52	(14)	58	(14)	54	(14)	54	(14)	61	(14)	56	(14)
		Three conditions of multimorbidity and two dimensions of frailty*						Three conditions of multimorbidity and two dimensions of frailty*					
		No, freq.	(%)	Yes, freq.	(%)	Total, freq.	(%)	No, freq.	(%)	Yes, freq.	(%)	Total, freq.	(%)
Total		16 983	(82)	3 803	(18)	20 813	(100)	14 367	(83)	2 837	(16)	17 214	(100)
Occupational group													
	High	4 029	(89)	475	(11)	4 505	(100)	3 977	(89)	485	(11)	4 465	(100)
	Middle	4 491	(83)	888	(16)	5 386	(100)	3 995	(82)	860	(18)	4 857	(100)
	Low	8 463	(77)	2 440	(22)	10 922	(100)	6 395	(81)	1 492	(19)	7 892	(100)
Age, years													
	25-44	5 378	(90)	600	(10)	5 981	(100)	3 651	(93)	291	(7)	3 943	(100)
	45-64	7 920	(80)	1 914	(19)	9 840	(100)	7 024	(84)	1 341	(16)	8 366	(100)
	65-74	2 449	(77)	714	(23)	3 168	(100)	2 472	(80)	618	(20)	3 093	(100)
	75-100	1 236	(68)	575	(32)	1 824	(100)	1 220	(67)	587	(32)	1 812	(100)
Mean (SD)		53	(14)	60	(14)	54	(14)	55	(14)	63	(13)	56	(14)

Abbreviations: freq., frequency; SD, standard deviation

*In total, 27 women and 10 men miss data on both measures of multimorbidity with frailty.

In total, 77% reported more than two and 62% more than three conditions of multimorbidity. Frailty with one impairment was identified in 41% and with two impairments in 18%. Table 3 shows the distribution of the combined measures across occupational groups stratified by sex.

Overall, 39% met the criteria of having at least two conditions of multimorbidity with one dimension of frailty (41% [n=8482 of 20813] of women, 37% [n=6378 of 17214] of men) and 17% met the criteria of three-condition multimorbidity with two dimensions of frailty (18% [n=3803 of 20813] of women, 16% [n=2837 of 17214] of men).

Proportions of multimorbidity with frailty increased with lower occupational rank and increasing age, in both sexes, regardless of definition. Most individuals with any definition of multimorbidity with frailty, were younger than 64 years.

Table 4. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) between occupational groups and multimorbidity with frailty, stratified by sex.

		Women				Men			
Age, years	**Occupational group**	**Two conditions of multimorbidity and one dimension of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
55	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
80	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.17)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
Age, years	**Occupational group**	**Three conditions of multimorbidity and two dimensions of frailty**							
		PR	**(95% CI)**	**PD**	**(95% CI)**	**PR**	**(95% CI)**	**PD**	**(95% CI)**
30	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
55	High	1.00		0.00		1.00		0.00	
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.07)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
80	High	1.00	(Ref.)	0.00	(Ref.)	1.00	(Ref.)	0.00	(Ref.)
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)

Table 4 shows prevalence differences and prevalence ratios for each definition of multimorbidity with frailty between occupational groups for women and men at the ages 30, 55, and 80 years.

Prevalence differences in percentage points (pp) for two-condition multimorbidity with one dimension of frailty between high and low occupational groups were largest in women at 30 years, 17 (14 to 20) pp and 55 years, 15 (13 to 17) pp, and for men at 55 years, 15 (13 to 17) pp and 80 years 14 (9 to 18) pp. The prevalence ratio for the low occupational group compared with the high occupational group, for two-condition multimorbidity with one dimension of frailty, was greatest in women at 30 years, 2.09 (1.76 to 2.47) and in men at 55 years, 1.60 (1.48 to 1.72). The prevalence ratio decreased in both sexes in high age and was at 80 years 1.05 (0.95 to 1.16) for women and 1.27 (1.15 to 1.39) for men.

Correspondingly, prevalence differences in percentage points between high and low occupational groups for three-condition multimorbidity with two dimensions of frailty, were largest in women at 30 years, 8 (CI: 6 to 10) pp and 55 years, 10 (CI: 8 to 11) pp and in men at 55 years 9 (CI: 8 to 11) pp and 80 years 6 (CI: 1 to 10) pp. Prevalence ratio, comparing the low

occupational group with the highest occupational group for three-conditions multimorbidity with two conditions of frailty, was greatest in women at 30 years, 3.59 (1.43 to 5.08) and in men at 55 years 2.05 (1.80 to 2.33). The prevalence ratio decreased in both sexes in high age and was at 80 years 1.16 (0.94 to 1.42) for women and 1.22 (1.04 to 1.44) for men.

DISCUSSION

Main results

In this adult population health study, multimorbidity with frailty was common as 39% met the criteria of two-condition multimorbidity plus one dimension of frailty and 17% met the criteria of three-condition multimorbidity plus two dimensions of frailty. Proportions increased with lower occupational group, higher age and female sex from 25 to 74 years, but was common across age groups in both sexes. Occupational inequalities were consistent in both sexes until high age, diminishing in women, while still present in men at age 80 years.

Comparison with existing literature

Investigating two measures of multimorbidity with frailty in one sample offers a unique direct comparison of occurrences and socioeconomic gradients. Lower overall prevalence for the stricter measure three-condition multimorbidity with two dimensions of frailty, is expected. Defining multimorbidity by three or more conditions differentiates into older age.[26 29] The joint measure multimorbidity and frailty, show the same tendency, as 62% of 75- to 100-year-olds met the criteria of at least two-condition multimorbidity with one dimension of frailty, while 32% reported three-condition multimorbidity with two dimensions of frailty. In line with individual studies on multimorbidity[4 24] and frailty,[25] most individuals with co-present multimorbidity and frailty are younger than 64 years.

A recent commentary[1] emphasized exploring multimorbidity guidelines and frailty as part of multimorbidity's complexity and overlap of multimorbidity and frailty has newly been reviewed.[28] A pooled prevalence of 16% (95% CI 12-21%) was reported for two conditions multimorbidity with the frailty phenotype among elderly,[28] while 39% in our study reported at least two conditions of multimorbidity with one dimension of frailty. The prevalence differences are likely explained by differences in methods. The articles included in the review studied age 60 years and older. Still, the prevalence of multimorbidity are low. All but one defined multimorbidity from lists of less than 12 conditions and prevalences are probably underestimated.[26 29] Frailty too was only operationalized with the biophysical model, while more people are expected to be detected using a multidimensional measure.

We have not identified studies on prevalence and social determinants of multimorbidity with frailty. Low social position,[18 19] older age,[18 20] and female sex[18 20] are known common determinants of multimorbidity and frailty. We therefore argue that the direction of the sociodemographic determinants in this study are as expected. The magnitudes of these gradients, however, have not been comparable with other studies.

Mechanisms to explain findings

The aggregation of ill health, multimorbidity and frailty included, in lower socioeconomic positions is explained by numerous theories. Overall, unequal distribution of power, income and

resources, result in fundamental different conditions of daily life yielding inequalities in health.[17] With regards to occupation, several mechanisms can explain associations to health outcomes. The higher occupational group is expected to have higher, more stable income,[35 39] more beneficial social networks,[39] and more autonomy and control[35 39] at work. Adverse working conditions such as exposure to toxic work environments[21] or demanding physical requirements[39] tend to cluster in lower occupational groups.[17] Persisting health inequalities in assumed egalitarian Nordic countries, is partly understood as mortality selection, where, given the well-developed health care and welfare systems, frail individuals survive, but likely end up in a low social position.[16] Further, smoking, overall morbidity and mortality decreases at a higher rate among higher than lower social groups.[16] In this study, the demographic age distribution explain the high number of 45- to 64-years old with co-present multimorbidity and frailty. Additionally, incidence of new conditions, is associated with count of conditions at baseline,[4] as well as age,[4] thus individuals in lower occupational groups may aggregate conditions faster. The bidirectional association of health and occupation, may explain higher occupational group prevalence ratios in younger individuals,[21] while lower ratios by increasing age are expected, since multimorbidity with frailty is more common[40] with advancing age. Finally, survival bias justifies diminishing occupational differences at age 80 years.

Strengths and limitations

Materials and methods meet the standards of studies on multimorbidity, frailty, and social health inequalities, strengthening this study. In multimorbidity studies, population-based health surveys are the most frequent study design,[41] and prevalence estimates from self-reports are justified when studying large samples.[26] Deriving the condition count multimorbidity measures from a complete list of single-entity conditions, is shown to yield proper prevalence estimates.[29] A multidimensional frailty measure agrees with an holistic, unrestricted on age, conceptual definition of frailty[14] and with common frailty scales, which share ability to show associations to age, sex and mortality.[20] In descriptive studies, any measure of socioeconomic position will reveal health inequalities, if such exists.[21] Occupation is an established marker for socioeconomic position,[21] in which this study had individual data classified to facilitate international comparison. Finally, socioeconomic differences are explored as both absolute and relative measures[16] and presented by sex.[18]

There are always limitations in secondary analysis of data collected a priori and not for the purpose of the current study. Measures of multimorbidity and frailty are also manifold, and operationalizations were adjusted to fit the available data. This challenges the external validity and comparability between studies, however, is sought reduced through transparency of morbidities included and construction of variables. A majority of included multimorbidity conditions do not contain information regarding duration. Thus, reported prevalence of multimorbidity may be overestimated and not represent true chronicity. It is recognized that frailty scales may differ in accuracy of detecting frailty in younger age groups,[10 20] however, frailty symptoms are of great clinical value regardless of age.[10 42] The accuracy of the frailty variables were not explored and frailty was measured solely as self-report, an approach that may underestimate overall prevalence[43] and overestimate proportion among women compared to men.[43]

Lastly, in the HUNT3 Survey participants were asked for their "main" occupation, which is not necessarily the current or longest lasting occupation, more commonly studied.[39] Younger than middle-aged may to some extent be misclassified in the lower occupational group, which will underestimate social differences in health among younger subjects. Occupational data may obscure current social context,[39] and underestimate socioeconomic inequalities. Thus, the study would have benefitted from exploring socioeconomic position with several indicators,[44] such as individual education and income or a household measure.

Attendance in the HUNT3 Survey varied by age, sex, and social position,[32] still, the HUNT study is considered representative for Norway as a whole[45] and the cohort follows trends in health development in western high-income countries.[46-48] Depression hindered participation,[32] which may yield underestimation of both multimorbidity and frailty. An overall bias towards healthy elders is probable, since eligibility depended on attendance at a screening station.

Implications for clinical practice and policy makers

This study aimed to quantify the total prevalence of adults in the general population who might need complex, multidisciplinary care assessed as the joint measure multimorbidity with frailty. In a clinical context, the definition of at least three-condition multimorbidity with two dimensions of frailty to detect individuals for whom to initiate a multimorbid approach to care, seems more feasible. Despite acknowledgement of the association of multimorbidity and frailty with age, sex, and socioeconomic position, guidelines and interventions have yet to take this into account in assessment and management for multimorbidity.[49] Based on literature and reproduction of social gradients in our study, we suggest that clinicians consider evaluation of multimorbidity and frailty in younger age groups with social context in mind. Further research on implementation of the multimorbid approach to care model and mortality is needed before recommending changing inclusion criteria in a guideline. Since multimorbidity is becoming the norm, the organization of health care should reform to fit person-centred, coordinated, multidisciplinary care.[6 10 50]To prevent cases of multimorbidity and frailty and minimize social discrepancies, both universal and targeted life cycle approaches seem necessary.[51]
Frailty is independently associated with mortality, adjusted for multimorbidity,[25] and is reversible.[52] Thus detection of frailty is relevant for both public health and clinical purposes.

Future research

Some forms of biases are possible for both multimorbidity, frailty and social position, and a careful interpretation of findings is warranted. However, multimorbidity with frailty is common in this general population and with occupational inequalities throughout adulthood, even with stricter definitions. This adds knowledge to the public health literature about the sociodemographic distribution of multimorbidity with frailty in younger age groups, as well as very old individuals. On this background, we recommend exploring the sociodemographic distribution of alternative measures on multimorbidity, including patterns, aiming to detect individuals suspected in high need of complex, multidisciplinary health care. Furthermore, such measurements can be compared as prognostic factors for health care utilization and mortality.

CONCLUSION

Multimorbidity with frailty are common from young adulthood onward, with consistent socioeconomic inequalities until 80 years old. Prevention will require a proportionate universal approach on social determinants of health throughout the entire life span. The crucial need for person-centered multimorbid approach to care that acknowledges social context, demands reforms in health care organizational structure, medical education, and treatment. Further research on competing measures of high-need multimorbidity and the association of these factors with health care utilization and mortality should be explored by socioeconomic position, age and sex.

FIGURES

Figure 1: Flowchart for sample selection: inclusion and exclusion criteria and missing data.

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COMPETING INTERESTS

None declared.

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AUTHOR CONTRIBUTIONS

KHV, ERS and KD conceptualized the study and all authors contributed to its design. KHV has analysed the data under supervision of ERS and all authors have contributed to interpreting the data. KHV wrote the original draft, which has been revised critically by ERS, KD and PB. All authors have read and approved the final version of the manuscript to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

LICENSE STATEMENT

PATIENT CONSENT

Participation in all parts of the HUNT3 Survey was voluntary, and written informed consent was obtained from all participants.

ETHICS APPROVAL

The Regional Committee for Medical and Health Research Ethics in Norway approved the current study (project no. 2014/2265).

DATA SHARING STATEMENT

To protect participants' privacy, HUNT Research Centre aims to limit storage of data outside HUNT databank and cannot deposit data in open repositories. HUNT databank has precise information on all data exported to different projects and are able to reproduce these on request. There are no restrictions regarding data export given approval of applications to HUNT Research Centre. For more information see: http://www.ntnu.edu/hunt/data

SUPPLEMENTARY FILES

Appendix A: Operationalizing socioeconomic position.

Appendix B: Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

Appendix C: Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational group and multimorbidity with frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

REFERENCES

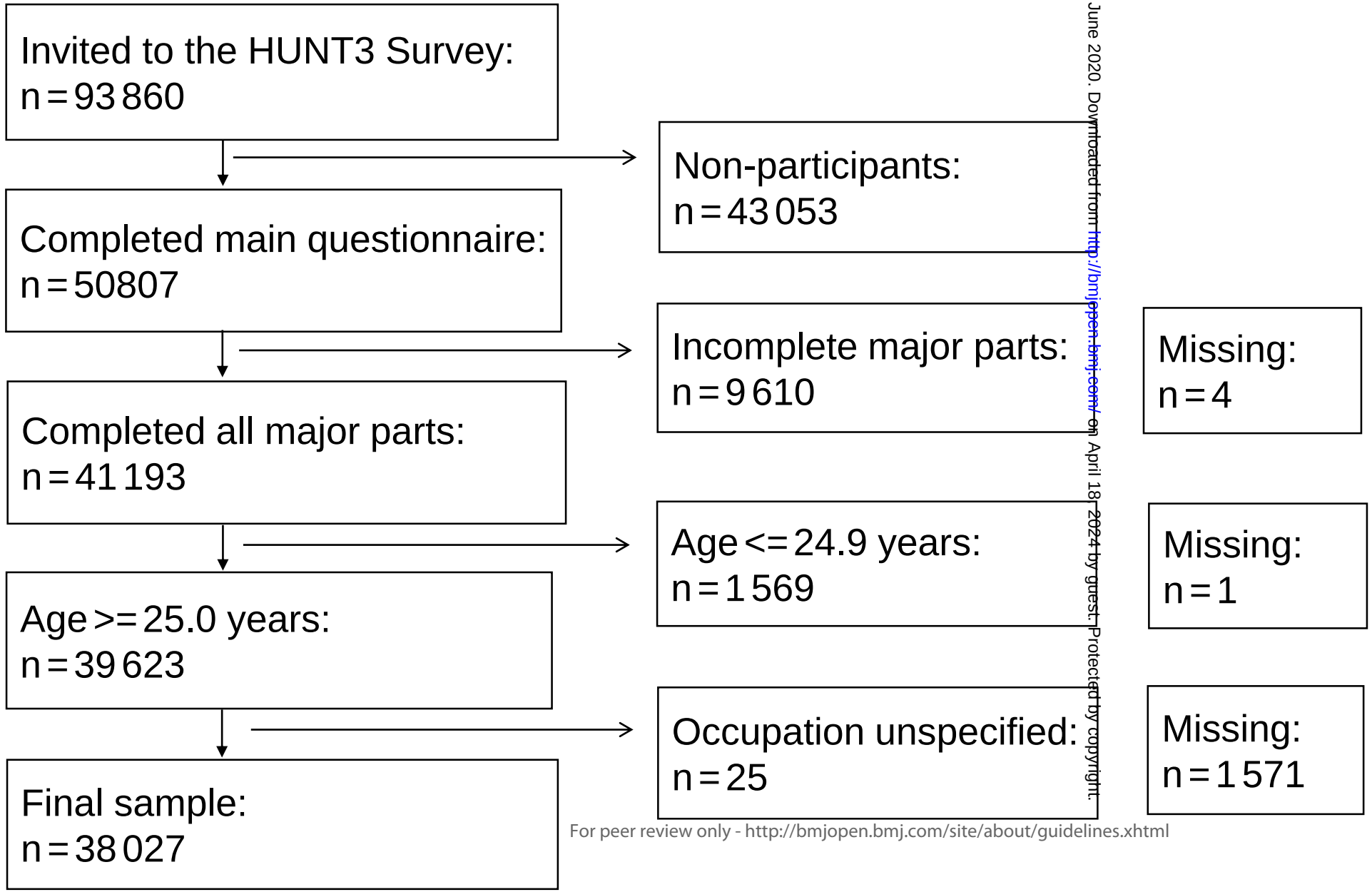
1. Nicholson K, Makovski TT, Griffith LE, et al. Multimorbidity and comorbidity revisited: refining the concepts for international health research. *J Clin Epidemiol* 2019;105:142-46. doi: 10.1016/j.jclinepi.2018.09.008 [published Online First: 2018/09/27]
2. van Oostrom SH, Gijsen R, Stirbu I, et al. Time Trends in Prevalence of Chronic Diseases and Multimorbidity Not Only due to Aging: Data from General Practices and Health Surveys. *PLoS One* 2016;11(8):e0160264. doi: 10.1371/journal.pone.0160264 [published Online First: 2016/08/03]
3. Uijen AA, van de Lisdonk EH. Multimorbidity in primary care: prevalence and trend over the last 20 years. *Eur J Gen Pract* 2008;14 Suppl 1(sup1):28-32. doi: 10.1080/13814780802436093 [published Online First: 2008/10/31]
4. van den Akker M, Buntinx F, Metsemakers JF, et al. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. *J Clin Epidemiol* 1998;51(5):367-75. doi: 10.1016/s0895-4356(97)00306-5 [published Online First: 1998/06/10]
5. Glynn LG, Valderas JM, Healy P, et al. The prevalence of multimorbidity in primary care and its effect on health care utilization and cost. *Fam Pract* 2011;28(5):516-23. doi: 10.1093/fampra/cmr013 [published Online First: 2011/03/26]
6. Wallace E, Salisbury C, Guthrie B, et al. Managing patients with multimorbidity in primary care. *BMJ* 2015;350:h176. doi: 10.1136/bmj.h176 [published Online First: 2015/02/04]
7. Guthrie B, Payne K, Alderson P, et al. Adapting clinical guidelines to take account of multimorbidity. *BMJ* 2012;345:e6341. doi: 10.1136/bmj.e6341 [published Online First: 2012/10/06]
8. Muth C, Kirchner H, van den Akker M, et al. Current guidelines poorly address multimorbidity: pilot of the interaction matrix method. *J Clin Epidemiol* 2014;67(11):1242-50. doi: 10.1016/j.jclinepi.2014.07.004 [published Online First: 2014/09/14]
9. Palmer K, Marengoni A, Forjaz MJ, et al. Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS). *Health Policy* 2018;122(1):4-11. doi: 10.1016/j.healthpol.2017.09.006 [published Online First: 2017/10/03]
10. National Institute for Health and Care Excellence. Multimorbidity: clinical assessment and management. London: National Institute for Health and Care Excellence (UK). 2016.
11. Schaink AK, Kuluski K, Lyons RF, et al. A scoping review and thematic classification of patient complexity: offering a unifying framework. *Journal of comorbidity* 2012;2:1-9. doi: 10.15256/joc.2012.2.15 [published Online First: 2012/10/10]
12. Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;56(3):M146-56. doi: 10.1093/gerona/56.3.m146 [published Online First: 2001/03/17]
13. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;1:323-36. doi: 10.1100/tsw.2001.58 [published Online First: 2003/06/14]
14. Gobbens RJ, Luijkx KG, Wijnen-Sponselee MT, et al. In search of an integral conceptual definition of frailty: opinions of experts. *J Am Med Dir Assoc* 2010;11(5):338-43. doi: 10.1016/j.jamda.2009.09.015 [published Online First: 2010/06/01]
15. Solfrizzi V, Scafato E, Lozupone M, et al. Biopsychosocial frailty and the risk of incident dementia: The Italian longitudinal study on aging. *Alzheimers Dement* 2019;15(8):1019-28. doi: 10.1016/j.jalz.2019.04.013 [published Online First: 2019/07/07]
16. Huijts T, Eikemo TA. Causality, social selectivity or artefacts? Why socioeconomic inequalities in health are not smallest in the Nordic countries. *Eur J Public Health* 2009;19(5):452-3. doi: 10.1093/eurpub/ckp103 [published Online First: 2009/07/10]
17. Commission on Social Determinants of Health. Closing the gap in a generation: health equity through action on the social determinants of health: final report of the commission on social determinants of health. Geneva2008:9.
18. Violan C, Foguet-Boreu Q, Flores-Mateo G, et al. Prevalence, determinants and patterns of multimorbidity in primary care: a systematic review of observational studies. *PLoS One* 2014;9(7):e102149. doi: 10.1371/journal.pone.0102149 [published Online First: 2014/07/23]

19. Franse CB, van Grieken A, Qin L, et al. Socioeconomic inequalities in frailty and frailty components among community-dwelling older citizens. *PLoS One* 2017;12(11):e0187946. doi: 10.1371/journal.pone.0187946 [published Online First: 2017/11/10]
20. Theou O, Brothers TD, Pena FG, et al. Identifying common characteristics of frailty across seven scales. *J Am Geriatr Soc* 2014;62(5):901-6. doi: 10.1111/jgs.12773 [published Online First: 2014/04/05]
21. Galobardes B, Lynch J, Smith GD. Measuring socioeconomic position in health research. *Br Med Bull* 2007;81-82(1):21-37. doi: 10.1093/bmb/ldm001 [published Online First: 2007/02/08]
22. Agborsangaya CB, Lau D, Lahtinen M, et al. Multimorbidity prevalence and patterns across socioeconomic determinants: a cross-sectional survey. *BMC Public Health* 2012;12:201. doi: 10.1186/1471-2458-12-201 [published Online First: 2012/03/21]
23. Szanton SL, Seplaki CL, Thorpe RJ, Jr., et al. Socioeconomic status is associated with frailty: the Women's Health and Aging Studies. *J Epidemiol Community Health* 2010;64(1):63-7. doi: 10.1136/jech.2008.078428 [published Online First: 2009/08/21]
24. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012;380(9836):37-43. doi: 10.1016/S0140-6736(12)60240-2 [published Online First: 2012/05/15]
25. Hanlon P, Nicholl BI, Jani BD, et al. Frailty and pre-frailty in middle-aged and older adults and its association with multimorbidity and mortality: a prospective analysis of 493 737 UK Biobank participants. *The Lancet Public health* 2018;3(7):e323-e32. doi: 10.1016/S2468-2667(18)30091-4 [published Online First: 2018/06/18]
26. Fortin M, Stewart M, Poitras ME, et al. A systematic review of prevalence studies on multimorbidity: toward a more uniform methodology. *Ann Fam Med* 2012;10(2):142-51. doi: 10.1370/afm.1337 [published Online First: 2012/03/14]
27. O'Caoimh R, Galluzzo L, Rodriguez-Laso A, et al. Prevalence of frailty at population level in European ADVANTAGE Joint Action Member States: a systematic review and meta-analysis. *Ann Ist Super Sanita* 2018;54(3):226-38. doi: 10.4415/ANN_18_03_10 [published Online First: 2018/10/05]
28. Vetrano DL, Palmer K, Marengoni A, et al. Frailty and Multimorbidity: A Systematic Review and Meta-analysis. *J Gerontol A Biol Sci Med Sci* 2019;74(5):659-66. doi: 10.1093/gerona/gly110 [published Online First: 2018/05/05]
29. Harrison C, Britt H, Miller G, et al. Examining different measures of multimorbidity, using a large prospective cross-sectional study in Australian general practice. *BMJ Open* 2014;4(7):e004694. doi: 10.1136/bmjopen-2013-004694 [published Online First: 2014/07/13]
30. von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg* 2014;12(12):1495-9. doi: 10.1016/j.ijsu.2014.07.013 [published Online First: 2014/07/22]
31. Krokstad S, Langhammer A, Hveem K, et al. Cohort Profile: the HUNT Study, Norway. *Int J Epidemiol* 2013;42(4):968-77. doi: 10.1093/ije/dys095 [published Online First: 2012/08/11]
32. Langhammer A, Krokstad S, Romundstad P, et al. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. *BMC Med Res Methodol* 2012;12:143. doi: 10.1186/1471-2288-12-143 [published Online First: 2012/09/18]
33. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway 1998.
34. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
35. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518
36. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
37. Sedgwick P. Relative risks versus odds ratios. *Bmj-British Medical Journal* 2014;348(feb07 2):g1407-g07. doi: ARTN g1407

10.1136/bmj.g1407

38. Norton EC, Miller MM, Kleinman LC. Computing Adjusted Risk Ratios and Risk Differences in Stata. *The Stata Journal: Promoting communications on statistics and Stata* 2018;13(3):492-509. doi: 10.1177/1536867x1301300304
39. Galobardes B, Shaw M, Lawlor DA, et al. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12. doi: 10.1136/jech.2004.023531 [published Online First: 2005/12/20]
40. Scanlan JP. Guest Editorial. *Chance* 2013;19(2):47-51. doi: 10.1080/09332480.2006.10722787 [published Online First: 02 Aug 2013]
41. Willadsen TG, Bebe A, Koster-Rasmussen R, et al. The role of diseases, risk factors and symptoms in the definition of multimorbidity - a systematic review. *Scand J Prim Health Care* 2016;34(2):112-21. doi: 10.3109/02813432.2016.1153242 [published Online First: 2016/03/10]
42. Schuurmans H, Steverink N, Lindenberg S, et al. Old or frail: what tells us more? *J Gerontol A Biol Sci Med Sci* 2004;59(9):M962-5. doi: 10.1093/gerona/59.9.m962 [published Online First: 2004/10/09]
43. Theou O, O'Connell MD, King-Kallimanis BL, et al. Measuring frailty using self-report and test-based health measures. *Age Ageing* 2015;44(3):471-7. doi: 10.1093/ageing/afv010 [published Online First: 2015/02/18]
44. Braveman PA, Cubbin C, Egerter S, et al. Socioeconomic status in health research: one size does not fit all. *JAMA* 2005;294(22):2879-88.
45. Holmen J, Midthjell K, Krüger Ø, et al. The Nord-Trøndelag Health Study 1995–97 (HUNT 2): objectives, contents, methods and participation. *Norsk epidemiologi* 2003;13(1):19-32.
46. NCD Risk Factor Collaboration (NCD-RisC). Rising rural body-mass index is the main driver of the global obesity epidemic in adults. *Nature* 2019;569(7755):260-64. doi: 10.1038/s41586-019-1171-x [published Online First: 2019/05/10]
47. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet* 2017;389(10064):37-55. doi: 10.1016/S0140-6736(16)31919-5 [published Online First: 2016/11/20]
48. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017;390(10113):2627-42. doi: 10.1016/S0140-6736(17)32129-3 [published Online First: 2017/10/17]
49. Smith SM, Soubhi H, Fortin M, et al. Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *BMJ* 2012;345:e5205. doi: 10.1136/bmj.e5205 [published Online First: 2012/09/05]
50. World Health Organization. Multimorbidity: Technical Series on Safer Primary Care. In: Organization WH, ed. Licence: CC BY-NC-SA 3.0 IGO. ed. Geneva.: World Health Organization, 2016:p. 4-5.
51. Marmot M, Goldblatt P, Allen J, et al. Fair Society, Healthy Lives.: The Marmot Review 2010.
52. Gill TM, Gahbauer EA, Allore HG, et al. Transitions between frailty states among community-living older persons. *Arch Intern Med* 2006;166(4):418-23. doi: 10.1001/archinte.166.4.418 [published Online First: 2006/03/01]

Fig. 1. Flowchart sample selection: inclusion and exclusion criteria and missing data.



Appendix A Operationalizing socioeconomic position using occupation.

In the HUNT3 Survey interview, all participants were asked: "What is/was the title of your main occupation?" Free-text answers were manually classified according to the *Standard Classifications of Occupations* by Statistics Norway,[1] which is based on the European Union's version of the *International Standard Classification of Occupations-88.*[2]

The standard categorize occupations according to skill level and specialization, degree of independence, and manual labor but not social position.[1] Occupations are coded with up to four digits, with increasing detail. One digit indicates major groups; two digits, submajor groups; three digits, minor groups; and four digits, unit groups. The minor occupational group was the highest level of detail available in the HUNT3 Survey.

Occupational socioeconomic position was operationalized using the European Socio-economic Classification scheme.[3] The full version of the scheme requires employment status and size of organization in addition to occupation to assign a class position. We used the simplified class scheme, based on minor occupational group only[3], as the HUNT3 Survey did not have data corresponding to employment status and size of organization. It is shown that the agreement between three-digit full and simplified version of this scheme is 79.7% for the total workforce.[3]

The syntax is available from https://www.iser.essex.ac.uk/archives/esec/matrices-and-syntax. It was performed using SPSS 25.0 (SPSS Inc., Chicago, IL, USA).

Table 1 gives details of transformation of data, discrepancies between the Norwegian and European Union standard and the allocated position in the full classification scheme. 2179 individuals had alterations to their occupational data to fit the syntax, 5.7% (2179/38027) of the total sample.

In the HUNT3 Survey data, the minor occupational group was a string variable. To perform the syntax, it had to be altered to a numeric variable. The string "011" changed to numeric value "11," which was manually corrected in the syntax. In the 3-digit variable, some participants were classified with 1 digit and 2 digits only. These were transformed to the corresponding 3-digit minor group, at the lowest level of detail, by manually adding suffix digits 0 or 00. This is in line with operationalizing of European Socio-economic Classification (see footnote table 1).[3]

Norwegian minor groups, which were not found in the European Union standard, were altered to the level of detail in which corresponding groups could be identified. These were *Standard Classifications of Occupations* by Statistics Norway codes: 112 (corresponding to 2 digits), 25 (corresponding to 1 digit), 251-6 (corresponding to 1 digit), 349 (corresponding to 2 digits), 631 (corresponding to 1 digit), 641 (corresponding to 1 digit), 735 (corresponding to 2 digits), and 745 (corresponding to 2 digits).

In total, 9 classes were created. To increase power and simplify interpretation, the full scheme was collapsed into a 3-class version, with “high” combining class 1 and 2, “middle” combining 3 to 6, and “low” combining 7 to 9. [3] The high occupational class represents large employers, higher-grade and lower-grade professionals, administrative and managerial occupations, higher-grade technician occupations, and supervisory occupations. The middle occupational class consist of small employers, self-employed individuals, lower supervisory occupations, and lower technician occupations. The low occupational class contain lower services, sales and clerical occupations, lower technical occupations, and routine occupations.

Table A1. The distribution of transformed occupational data and discrepancies between the Norwegian and International Standard Classifications of Occupations, and allocation in the European Socio-economic Classification scheme.

Standard Classifications of Occupations		**European Socio-economic**		
Norwegian	**International**	**Classification scheme**	***n***	**%**
1	100	1	262	(0.69)
011 (=num 11)	011=11	3	134	(0.35)
112*	→ 11=110	1	31	(0.08)
12	120	1	73	(0.19)
13	130	4	20	(0.05)
2	200	1	10	(0.03)
21	210	1	10	(0.03)
22	220	1	1	(0.00)
23	230	2	27	(0.07)
24	240	1	9	(0.02)
25	→ 2=200	1	4	(0.01)
251*	→ 2=200	1	296	(0.78)
252*	→ 2=200	1	48	(0.13)
253*	→ 2=200	1	20	(0.05)
254*	→ 2=200	1	138	(0.36)
255*	→ 2=200	1	64	(0.17)
256*	→ 2=200	1	46	(0.12)
3	300	3	39	(0.10)
31	310	2	37	(0.10)
33	330	3	241	(0.63)
34	340	3	45	(0.12)
349*	→34=340	3	160	(0.42)
4	400	3	1	(0.00)
41	410	3	1	(0.00)
42	420	3	1	(0.00)
5	500	7	1	(0.00)
51	510	7	8	(0.02)
61	610	5	4	(0.01)
631*	→6=600	5	93	(0.24)
641*	→6=600	5	99	(0.26)
7	700	8	20	(0.05)
71	710	8	1	(0.00)
72	720	8	6	(0.02)
73	730	6	1	(0.00)
735*	→73=730	6	38	(0.10)
74	740	8	1	(0.00)
745*	→74=740	8	46	(0.12)
8	800	9	62	(0.16)
81	810	9	38	(0.10)
82	820	9	35	(0.09)
83	830	9	6	(0.02)
9	900	9	1	(0.00)
93	930	9	1	(0.00)
Sum			2179	(5.73)

Bold* = Divergence of *Standard Classifications of Occupations* by Statistics Norway from the European Union's version of *The International Standard Classification of Occupations-88*.

References

1. Statistics Norway. Standard Classification of Occupations. Oslo/Kongsvinger: Statistics Norway, 1998.
2. International Labour Organization (ILO). The International Standard Classification of Occupations, ISCO-88 [Webpage]. 1988 [updated 18.09.2004. Available from: https://www.ilo.org/public/english/bureau/stat/isco/isco88/index.htm accessed 24.05. 2019.
3. Rose D, Harrison E. The european socio-economic classification: A new social class schema for comparative European research. *Eur Soc* 2007;9(3):459-90. doi: 10.1080/14616690701336518

Appendix B

Construction of chronic, single-entities conditions from data in the HUNT3 Survey, by questionnaires and measurements.

ORIGINAL QUESTIONNAIRE, ENGLISH VERSION

Main questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=129b68c3-520c-457f-8b98-02c49219b2ee&groupId=140075

Sex- and age-specific questionnaire

https://www.ntnu.edu/c/document_library/get_file?uuid=35ae2816-4155-4b64-a259-770946fa46d4&groupId=140075

GENERAL COMMENTS

Chronicity

Chronicity was defined by either 1: duration (3 months or longer), 2: causing functional limitation (physical, mental, social) or 3: requiring health care management (pharmacological or not, primary or specialist care),[1] or 4: chronicity was assumed based on medical knowledge and clinical experience.

Missing

In variables with index questions and cluster text, missing was in general corrected for affirmed index question and regarded as “no” if replied to any alternative to any of the other questions in the block. Information on missing is also collected from the HUNT Databank.

MAIN QUESTIONNAIRE

Hearing impairment

Index question: “Do you suffer from longstanding (at least 1 year) illness or injury of a physical or psychological nature that impairs your functioning in your daily life?” Yes, no. Options on follow-up question combined condition type (motor, vision, hearing, somatic, and psychiatric) and severity (slight, moderate, and severe).

Included with hearing impairment were those who reported chronic disease and moderate to severe hearing impairment.

"20 Diseases": Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis

Cluster text: "Have you had or do you have any of the following:
Myocardial infarction, angina pectoris, heart failure, other heart disease, stroke or brain haemorrhage, kidney disease, asthma, chronic bronchitis, emphysema or chronic obstructive pulmonary disease, diabetes, psoriasis, eczema on hands, cancer, epilepsy, rheumatoid arthritis, ankylosing spondylitis, sarcoidosis, osteoporosis, fibromyalgia and osteoarthritis?"
Separate tick boxes for each diagnosis: Yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

Sex- and age-differentiated questionnaire

Headache

Seven questions in one block. Question 1: "Have you had headaches in the last year?" Yes/no.

Migraine without aura

Of those who affirmed headache last year, migraine without aura was constructed from three of seven questions:

1. "What is the average strength of your headaches?" 1=Mild, 2=Moderate, 3=Strong.
   Recoded to dichotomous variable, where 1=Moderate/Strong.
2. "How long does the headache usually last?" 1=Less than 4 hours, 2=4 hours - 1 day, 3=1 - 3 days, 4= More than 3 days.
   Recoded to dichotomous variable, where 1= Less than 4 hours – 3 days.
3. Cluster text: "Are the headaches usually characterized or accompanied by
   - Throbbing/thumping pain?" Yes, no.
   - Pain on one side of the head?" Yes, no.
   - Worsening with physical activity?" Yes, no.
   - Nausea and/or vomiting?" Yes, no.
   - Hypersensitivity to light and/or noise?" Yes, no.

Included with migraine: were those who affirmed to headache lasting 0 to 72 hours and at least two of four characteristics (pulsating quality, unilateral location, moderate/severe pain intensity, or aggravation by physical activity) and during headache having at least one of two accompanying symptoms (nausea and/or vomiting or increased sensitivity to light and/or noise).[2]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic headache

Of those who affirmed headache last year, chronic headache was constructed from two of seven questions:

1. "If yes (headache in the last year): What type of headache? Migraine, other."
   The HUNT Databank created two variables with range 1: 1) migraine and 2) other headache.
2. "Average number of days a month with headaches:"
   1=Less than 1 day, 2=1-6 days, 3=7-14 days, 4=More than 14 days.
   Recoded to dichotomous variable, where 1= More than 14 days.

Included as case with chronic headache were those reporting "other" type of headache and an average frequency of more than 14 days per month.
Chronicity is assumed based on medical knowledge and clinical experience.

Pain

Index question: "In the last year, have you had pain or stiffness in muscles or joints that has lasted at least 3 consecutive months?" Yes, no.
The follow-up question "If yes: Where have you had this pain or stiffness?" was combined with a figure with arrows and tick boxes at nine locations (neck, upper back, lower back, shoulder, elbow, hand, hip, knee and ankle/foot).

Chronic widespread pain

Dichotomous variables were made for each major body area: 1) Trunk (neck, upper and lower back),
2) Upper limb (shoulder, elbow, hand), and 3) Lower limb (hip, knee, foot/ancle), where 1=At least one painful location. A sum (row total) score variable was made for the major body areas and dichotomized, where 1=3, that is one pain in each major body area.
Of those who affirmed to pain or stiffness that has lasted more than three consecutive months, chronic widespread pain was defined as pain at more than three sites in all major body areas (trunk, upper and lower limbs) for more than three months in the last year.[3]

Chronic, local pain

Of those who affirmed to pain or stiffness that has lasted more than three consecutive months,
chronic, local pain was defined as pain in the neck or upper back or lower back or shoulder or elbow or hand or hip or knee or ancle/foot, excluding presence of chronic widespread pain, generating nine dichotomous variables.

Thyroidal disease

Cluster text: "Has it ever been verified that you have/have had hypothyroidism or hyperthyroidism?" Separate tick boxes for each condition (yes, no), generating two dichotomous variables, 1=Yes.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.
Chronicity is assumed based on medical knowledge and clinical experience.

Irritable bowel syndrome

Index question: “Have you had stomach pain or discomfort in the last 12 months?” Answers: Yes, much; yes, a little; no. Irritable bowel syndrome was further constructed from four of six follow-up questions: “If yes:
“In the last 3 months, have you had this as often as 1 day a week for at least 3 weeks?” Yes, no.
“Is the pain/discomfort relieved by having a bowel movement?” Yes, no.
“Is the pain/discomfort related to more frequent or less frequent bowel movements than normal?” Yes,no.
“Is the pain/discomfort related to the stool being softer or harder than usual?” Yes, no.

Included with irritable bowel syndrome were those who affirmed little or much stomach pain or discomfort in the last year, who for as often as 1 day a week for at least 3 weeks in the last 3 months have had at least two of the following: pain/discomfort relieved by having a bowel movement, related to altered frequency of bowel movements, or related to altered stool appearance, resembling a modified version of the Rome criteria.[4 5]

Gastro-oesophageal reflux disease

Cluster text: “To what degree have you had the following problems in the last 12 months?” Options combined type (nausea, heartburn/acid regurgitation, diarrhea, constipation, alternating constipation and diarrhea, and bloating) and frequency (never, a little, or much). Generated one dichotomous variable, heartburn, where 1=Much.
Gastro-oesophageal reflux disease is defined as much heartburn/acid regurgitation in the last 12 months.[6]

Anxiety

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed a total score for anxiety (HADS-A), if all 7 anxiety items were answered.
Anxiety was defined as HADS-A score >=8/21, indicating mild or possible anxiety.[8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Depression

Instrument variable: Hospital Anxiety and Depression Scale.[7] Every other statement of 14 statements covers symptoms on anxiety and depression and is scored 0-3. The HUNT Databank constructed total score depression (HADS-D), if all 7 depression items were answered.
Depression was defined as HADS-D score >=8/21, indicating mild or possible depression.[8-10]
Chronicity is assumed based on medical knowledge and clinical experience.

Chronic insomnia

There were nine questions on sleeping pattern in one cluster, including three concerning insomnia. Initial text: “How often in the last 3 months have you
“Had difficulty falling asleep at night?” Never/seldom, sometimes, several times a week.
“Woken up repeatedly during the night?” Never/seldom, sometimes, several times a week.

"Woken too early and couldn't get back to sleep?" Never/seldom, sometimes, several times a week.
Chronic insomnia was defined as in the last 3 months, several times a week, having difficulty falling asleep at night and waking up repeatedly during the night, and waking up too early. A modified version of the diagnostic criteria for insomnia in the International Classification of Sleep Disorders.[11]

Alcohol use disorder

Instrument variable: Cut down/Annoyed/Guilty/Eye-opener, also known as the CAGE questionnaire.12 The CAGE questionnaire is a 4-item scale with scores of 0-1. A summary variable was created and dichotomized in which a score of 1 indicates >=2 positive answers.
Alcohol use disorder was defined as CAGE score greater than 2.[13]
Chronicity is assumed based on medical knowledge and clinical experience.

Dental health problem

"How would you say your dental health is?" Very, bad, ok, good, very good.
Dental health problems were defined as self-reported bad or very bad dental health.
Chronicity is assumed based on medical knowledge and clinical experience.

Menopausal hot flashes

Asked to women older than 30 years only.
Two questions were used to define menopausal illness:
"Do you have/have you had hot flashes due to menopause?" During the day, during the night, day and night, haven't had any.
"If you have had hot flashes, how would you describe them?" Very intense, moderately intense, hardly noticeable.
Included with menopausal hot flashes were those who reported hot flashes occurring daily and/or nightly and of at least moderate severity.
Chronicity is assumed based on medical knowledge and clinical experience.

Nocturia

Age group 20-29 years were excluded.
One question on nocturia, identical to that of the International Prostate Symptom Scale (IPSS), was asked to men and women older than 30 years.
"How many times do you get up during the night to urinate?" None, 1 time, 2 times, 3 times, 4 times, 5 times or more.
Nocturia was defined as two or more voids per night.[14]
Chronicity is assumed based on medical knowledge and clinical experience.

Urine incontinence

Men 20-29 years were excluded.
Instrument variable: The Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) questionnaire.[15]
Index question: Do you have involuntary loss of urine? Yes, no.
Urine incontinence was constructed from two of six follow up questions. "If yes":

"How often do you have involuntary loss of urine?" Less than once a month, once or more per month, once or more per week, every day and/or night
"How much urine do you leak each time?" Drops or little, small amount, large amounts.

Self-reported frequency and volume of leakage were multiplied to obtain the validated 4-level Sandvik Severity Index, categorizing incontinence as slight, moderate, severe, and very severe.[15]
Urine incontinence were included if severe to very severe.
Chronicity is assumed based on medical knowledge and clinical experience.

Prostate symptoms

Asked of men older than 30 years only.
Instrument variable: The International Prostate Symptom Scale [16] was slightly modified in HUNT3,[17] becoming a 7-item scale with scores of 0-5 per question.
Included were prostate symptoms of at least moderate severity, i.e. summary score >= 8 points.[16]
Chronicity is assumed based on medical knowledge and clinical experience.

Eye diseases

The age group 20-29 years were excluded.
Cluster text: "Do you have any of the following eye conditions?" Cataract, glaucoma, and macula degeneration. Separate tick boxes, yes, no.
For each diagnosis, included were those who affirmed to have or have had the diagnosis.

Measurements

Obesity

HUNT Databank constructed the BMI variable, defined as (weight in kg)/(height in m2).
Obesity was defined as either BMI>=35 or a BMI 25-34.9 and an increased waist circumference (>= 88 cm for females; >= 102 cm for males).18 19
Chronicity is assumed based on medical knowledge and clinical experience.

Hypertension

Blood pressure in HUNT3 is measured three times at one consultation. The mean of measurement 2 and 3 is calculated by HUNT Databank.
Hypertension was defined as measured mean systolic BP>= 180 mmHg or diastolic BP >= 110 mmHg or reporting use of antihypertensive medications, excluding self-reported cardiovascular disease, diabetes, or kidney disease, and excluding extreme measures.
Chronicity is assumed based on medical knowledge and clinical experience.

Hypercholesterolemia

Hypercholesterolemia was defined as total-cholesterol >= 8 mmol/L.[20]
Chronicity is assumed based on medical knowledge and clinical experience.

References

1. Goodman RA, Posner SF, Huang ES, et al. Defining and measuring chronic conditions: imperatives for research, policy, program, and practice. *Prev Chronic Dis* 2013;10:E66. doi: 10.5888/pcd10.120239 [published Online First: 2013/04/27]
2. Hagen K, Zwart JA, Aamodt AH, et al. The validity of questionnaire-based diagnoses: the third Nord-Trondelag Health Study 2006-2008. *J Headache Pain* 2010;11(1):67-73. doi: 10.1007/s10194-009-0174-7 [published Online First: 2009/12/01]
3. Mundal I, Grawe RW, Bjorngaard JH, et al. Prevalence and long-term predictors of persistent chronic widespread pain in the general population in an 11-year prospective study: the HUNT study. *BMC Musculoskelet Disord* 2014;15:213. doi: 10.1186/1471-2474-15-213 [published Online First: 2014/06/22]
4. Hammer J, Talley NJ. Diagnostic criteria for the irritable bowel syndrome. *Am J Med* 1999;107(5A):5S-11S. doi: 10.1016/s0002-9343(99)00276-4 [published Online First: 1999/12/10]
5. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. *Gastroenterology* 2006;130(5):1480-91. doi: 10.1053/j.gastro.2005.11.061 [published Online First: 2006/05/09]
6. Ness-Jensen E, Lindam A, Lagergren J, et al. Changes in prevalence, incidence and spontaneous loss of gastro-oesophageal reflux symptoms: a prospective population-based cohort study, the HUNT study. *Gut* 2012;61(10):1390-7. doi: 10.1136/gutjnl-2011-300715 [published Online First: 2011/12/23]
7. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361-70. doi: 10.1111/j.1600-0447.1983.tb09716.x [published Online First: 1983/06/01]
8. Mykletun A, Stordal E, Dahl AA. Hospital Anxiety and Depression (HAD) scale: factor structure, item analyses and internal consistency in a large population. *Br J Psychiatry* 2001;179:540-4. doi: 10.1192/bjp.179.6.540 [published Online First: 2001/12/04]
9. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52(2):69-77. doi: 10.1016/s0022-3999(01)00296-3 [published Online First: 2002/02/08]
10. Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. *J Psychosom Res* 1997;42(1):17-41. [published Online First: 1997/01/01]
11. Medicine AAoS. The international classification of sleep disorders: diagnostic and coding manual: American Acad. of Sleep Medicine 2005.
12. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA* 1984;252(14):1905-7. doi: 10.1001/jama.252.14.1905 [published Online First: 1984/10/12]
13. Skogen JC, Overland S, Knudsen AK, et al. Concurrent validity of the CAGE questionnaire. The Nord-Trondelag Health Study. *Addict Behav* 2011;36(4):302-7. doi: 10.1016/j.addbeh.2010.11.010 [published Online First: 2010/12/21]
14. Tikkinen KA, Johnson TM, 2nd, Tammela TL, et al. Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol* 2010;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080 [published Online First: 2009/04/14]
15. Sandvik H, Seim A, Vanvik A, et al. A severity index for epidemiological surveys of female urinary incontinence: comparison with 48-hour pad-weighing tests. *Neurourol Urodyn* 2000;19(2):137-45. [published Online First: 2000/02/19]
16. Barry MJ, Fowler FJ, Jr., O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549-57; discussion 64. doi: 10.1016/s0022-5347(17)36966-5 [published Online First: 1992/11/11]
17. HUNT Databank. International Prostate Symptom Scale in HUNT3 Questionnaire 2 [Webpage]. Levanger: HUNT Databank; 2019 [cited 2019 05.20.]. Available from: https://hunt-db.medisin.ntnu.no/hunt-db/#/instrumentpart/45_11 2019.
18. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79(3):379-84. doi: 10.1093/ajcn/79.3.379 [published Online First: 2004/02/27]
19. Perreault L. Obesity in adults: Prevalence, screening, and evaluation. Waltham, MA: UpToDate 2018.
20. Helsedirektoratet. Nasjonal faglig retningslinje for individuell primærforebygging av hjerte-og karsykdommer, kortversjon, IS-1675. In: Helsedirektoratet, ed., 2009.

Appendix C

Table C1. Prevalence ratios (PR) and prevalence differences (PD) with 95% confidence intervals (CI) for the association between occupational group and multimorbidity with frailty, stratified by sex, age 25 to 100 years in 5-year intervals.

*Occup. = occupational.

Two conditions of multimorbidity and one dimension of frailty

Age,	Occup.*	Female				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.01, 1.79)	0.05	(0.00, 0.09)	0.81	(0.55, 1.20)	-0.03	(-0.08, 0.03)
	Low	2.20	(1.73, 2.81)	0.17	(0.12, 0.21)	1.19	(0.86, 1.65)	0.03	(-0.02, 0.08)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.11, 1.65)	0.06	(0.02, 0.09)	0.93	(0.70, 1.23)	-0.01	(-0.06, 0.03)
	Low	2.09	(1.76, 2.47)	0.17	(0.14, 0.20)	1.32	(1.04, 1.67)	0.05	(0.01, 0.09)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.36	(1.19, 1.55)	0.06	(0.04, 0.09)	1.04	(0.85, 1.27)	0.01	(-0.03, 0.04)
	Low	1.97	(1.75, 2.20)	0.17	(0.15, 0.20)	1.43	(1.22, 1.68)	0.07	(0.04, 0.10)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(1.22, 1.47)	0.07	(0.05, 0.09)	1.14	(0.99, 1.31)	0.03	(0.00, 0.05)
	Low	1.84	(1.70, 2.00)	0.17	(0.15, 0.19)	1.52	(1.35, 1.70)	0.09	(0.07, 0.12)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.21, 1.42)	0.07	(0.05, 0.09)	1.23	(1.11, 1.36)	0.04	(0.02, 0.07)
	Low	1.72	(1.60, 1.84)	0.17	(0.15, 0.19)	1.58	(1.44, 1.72)	0.11	(0.09, 0.13)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.27	(1.17, 1.37)	0.07	(0.05, 0.10)	1.29	(1.18, 1.41)	0.06	(0.04, 0.09)
	Low	1.59	(1.49, 1.70)	0.16	(0.14, 0.18)	1.60	(1.48, 1.73)	0.13	(0.11, 0.15)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.22	(1.13, 1.31)	0.07	(0.04, 0.09)	1.34	(1.23, 1.45)	0.08	(0.06, 0.11)
	Low	1.48	(1.38, 1.58)	0.15	(0.13, 0.17)	1.60	(1.48, 1.72)	0.15	(0.13, 0.17)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(1.08, 1.25)	0.06	(0.03, 0.09)	1.35	(1.25, 1.46)	0.10	(0.08, 0.13)
	Low	1.37	(1.29, 1.46)	0.13	(0.11, 0.16)	1.56	(1.46, 1.68)	0.16	(0.14, 0.18)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.11	(1.03, 1.19)	0.04	(0.02, 0.07)	1.35	(1.26, 1.45)	0.11	(0.09, 0.14)
	Low	1.27	(1.20, 1.35)	0.11	(0.09, 0.14)	1.51	(1.41, 1.61)	0.17	(0.14, 0.19)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.05	(0.98, 1.14)	0.03	(-0.01, 0.06)	1.32	(1.24, 1.42)	0.12	(0.09, 0.15)
	Low	1.19	(1.11, 1.27)	0.09	(0.06, 0.12)	1.43	(1.35, 1.53)	0.16	(0.14, 0.19)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.01	(0.92, 1.10)	0.00	(-0.05, 0.05)	1.28	(1.19, 1.38)	0.12	(0.09, 0.16)
	Low	1.11	(1.03, 1.21)	0.06	(0.02, 0.10)	1.35	(1.25, 1.45)	0.15	(0.12, 0.19)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.96	(0.86, 1.08)	-0.02	(-0.09, 0.05)	1.23	(1.12, 1.35)	0.12	(0.06, 0.17)
	Low	1.05	(0.95, 1.16)	0.03	(-0.03, 0.09)	1.27	(1.15, 1.39)	0.14	(0.09, 0.18)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.93	(0.81, 1.06)	-0.05	(-0.14, 0.04)	1.17	(1.04, 1.32)	0.10	(0.03, 0.17)
	Low	1.00	(0.89, 1.13)	0.00	(-0.08, 0.08)	1.19	(1.06, 1.33)	0.11	(0.04, 0.18)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.90	(0.77, 1.05)	-0.07	(-0.18, 0.04)	1.12	(0.98, 1.29)	0.08	(-0.01, 0.17)
	Low	0.96	(0.85, 1.10)	-0.03	(-0.12, 0.07)	1.12	(0.98, 1.27)	0.08	(-0.01, 0.16)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.88	(0.74, 1.05)	-0.09	(-0.22, 0.03)	1.08	(0.93, 1.24)	0.06	(-0.05, 0.16)
	Low	0.94	(0.82, 1.08)	-0.05	(-0.15, 0.06)	1.06	(0.93, 1.22)	0.05	(-0.06, 0.15)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	0.86	(0.72, 1.04)	-0.11	(-0.25, 0.03)	1.04	(0.90, 1.20)	0.03	(-0.08, 0.15)
	Low	0.92	(0.80, 1.06)	-0.07	(-0.18, 0.05)	1.02	(0.89, 1.17)	0.02	(-0.09, 0.13)

Three conditions of multimorbidity and two dimensions of frailty

Age,	Occup.*	Female				Men			
years	group	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
25	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.74	(1.60, 4.71)	0.04	(0.02, 0.06)	1.15	(0.57, 2.32)	0.01	(-0.02, 0.03)
	Low	4.24	(2.61, 6.89)	0.07	(0.05, 0.10)	1.36	(0.74, 2.51)	0.01	(-0.01, 0.04)
30	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	2.31	(1.56, 3.40)	0.04	(0.02, 0.06)	1.29	(0.77, 2.17)	0.01	(-0.01, 0.03)
	Low	3.59	(2.53, 5.08)	0.08	(0.06, 0.10)	1.60	(1.02, 2.51)	0.02	(0.00, 0.04)
35	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.98	(1.51, 2.59)	0.04	(0.03, 0.06)	1.41	(0.97, 2.05)	0.02	(0.00, 0.04)
	Low	3.06	(2.41, 3.90)	0.09	(0.07, 0.11)	1.81	(1.31, 2.50)	0.04	(0.02, 0.05)
40	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.73	(1.43, 2.09)	0.04	(0.03, 0.06)	1.51	(1.16, 1.96)	0.03	(0.01, 0.04)
	Low	2.63	(2.23, 3.11)	0.10	(0.08, 0.11)	1.97	(1.57, 2.47)	0.05	(0.04, 0.07)
45	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.55	(1.33, 1.79)	0.04	(0.03, 0.06)	1.58	(1.30, 1.91)	0.04	(0.02, 0.05)
	Low	2.29	(2.01, 2.60)	0.10	(0.09, 0.11)	2.07	(1.75, 2.44)	0.07	(0.05, 0.08)
50	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.41	(1.23, 1.61)	0.04	(0.02, 0.06)	1.62	(1.38, 1.89)	0.05	(0.03, 0.06)
	Low	2.01	(1.78, 2.26)	0.10	(0.09, 0.11)	2.09	(1.82, 2.40)	0.08	(0.07, 0.09)
55	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.31	(1.14, 1.50)	0.04	(0.02, 0.06)	1.62	(1.40, 1.87)	0.06	(0.04, 0.07)
	Low	1.78	(1.59, 2.00)	0.10	(0.08, 0.11)	2.05	(1.80, 2.33)	0.09	(0.08, 0.11)
60	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.24	(1.09, 1.41)	0.04	(0.01, 0.06)	1.59	(1.39, 1.83)	0.07	(0.05, 0.08)
	Low	1.60	(1.43, 1.79)	0.09	(0.07, 0.11)	1.94	(1.71, 2.20)	0.10	(0.09, 0.12)
65	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(1.05, 1.35)	0.03	(0.01, 0.06)	1.54	(1.35, 1.75)	0.07	(0.05, 0.09)
	Low	1.45	(1.30, 1.62)	0.08	(0.06, 0.10)	1.79	(1.59, 2.01)	0.11	(0.09, 0.13)
70	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(1.02, 1.34)	0.04	(0.01, 0.06)	1.46	(1.29, 1.65)	0.08	(0.05, 0.10)
	Low	1.33	(1.18, 1.50)	0.07	(0.04, 0.10)	1.61	(1.44, 1.80)	0.10	(0.08, 0.12)
75	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.16	(0.98, 1.37)	0.04	(0.00, 0.08)	1.36	(1.19, 1.56)	0.07	(0.04, 0.11)
	Low	1.23	(1.06, 1.44)	0.06	(0.02, 0.09)	1.41	(1.25, 1.60)	0.09	(0.06, 0.11)
80	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.17	(0.94, 1.47)	0.05	(-0.02, 0.11)	1.26	(1.06, 1.50)	0.07	(0.02, 0.11)
	Low	1.16	(0.94, 1.42)	0.04	(-0.01, 0.10)	1.22	(1.04, 1.44)	0.06	(0.01, 0.10)
85	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.19	(0.88, 1.61)	0.06	(-0.04, 0.15)	1.16	(0.92, 1.46)	0.05	(-0.03, 0.13)
	Low	1.09	(0.83, 1.44)	0.03	(-0.05, 0.11)	1.05	(0.83, 1.31)	0.01	(-0.06, 0.09)
90	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.23	(0.83, 1.82)	0.07	(-0.06, 0.21)	1.06	(0.79, 1.43)	0.02	(-0.09, 0.14)
	Low	1.04	(0.72, 1.50)	0.01	(-0.10, 0.13)	0.89	(0.66, 1.19)	-0.04	(-0.15, 0.07)
95	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.28	(0.77, 2.10)	0.09	(-0.09, 0.27)	0.97	(0.68, 1.40)	-0.01	(-0.18, 0.15)
	Low	1.00	(0.63, 1.59)	0.00	(-0.16, 0.16)	0.76	(0.53, 1.09)	-0.11	(-0.27, 0.04)
100	High	1.0	(Ref.)	0.0	(Ref.)	1.0	(Ref.)	0.0	(Ref.)
	Middle	1.34	(0.72, 2.47)	0.12	(-0.12, 0.35)	0.90	(0.60, 1.36)	-0.05	(-0.27, 0.16)
	Low	0.96	(0.54, 1.73)	-0.01	(-0.22, 0.19)	0.65	(0.42, 0.99)	-0.19	(-0.39, 0.01)

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Title and abstract			
Title	#1a	Indicate the study's design with a commonly used term in the title or the abstract	1
Abstract	#1b	Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background / rationale	#2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	#3	State specific objectives, including any prespecified hypotheses	3
Methods			

Study design	#4	Present key elements of study design early in the paper	3-4
Setting	#5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4
Eligibility criteria	#6a	Give the eligibility criteria, and the sources and methods of selection of participants.	3-4
	#7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources / measurement	#8	For each variable of interest give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Give information separately for for exposed and unexposed groups if applicable.	4 + appendix B
Bias	#9	Describe any efforts to address potential sources of bias	5
Study size	#10	Explain how the study size was arrived at	NA, data collected a priori, informal assesment
Quantitative variables	#11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	5
Statistical methods	#12a	Describe all statistical methods, including those used to control for confounding	5
Statistical methods	#12b	Describe any methods used to examine subgroups and interactions	5
Statistical methods	#12c	Explain how missing data were addressed	5
Statistical methods	#12d	If applicable, describe analytical methods taking account of sampling strategy	N/A

Statistical methods	#12e	Describe any sensitivity analyses	N/A
Results			
Participants	#13a	Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Give information separately for for exposed and unexposed groups if applicable.	3-5, fig. 1
Participants	#13b	Give reasons for non-participation at each stage	Fig. 1
Participants	#13c	Consider use of a flow diagram	Fig. 1
Descriptive data	#14a	Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Give information separately for exposed and unexposed groups if applicable.	5-6
Descriptive data	#14b	Indicate number of participants with missing data for each variable of interest	6, Tab. 2
Outcome data	#15	Report numbers of outcome events or summary measures. Give information separately for exposed and unexposed groups if applicable.	4
Main results	#16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	We only gave adjusted estimates, p.6
Main results	#16b	Report category boundaries when continuous variables were categorized	6
Main results	#16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A, we used postestimation commands to obtain ratios and differences

Other analyses	#17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	5, Appendix c
Discussion			
Key results	#18	Summarise key results with reference to study objectives	8
Limitations	#19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	9
Interpretation	#20	Give a cautious overall interpretation considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	9
Generalisability	#21	Discuss the generalisability (external validity) of the study results	9
Other Information			
Funding	#22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	10